

PREŽIVETJE BOLNIKOV Z RAKOM V SLOVENIJI
CANCER PATIENTS SURVIVAL IN SLOVENIA

1983–1997

VERA POMPE - KIRN BRANKO ZAKOTNIK VESNA ZADNIK



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CANCER PATIENTS SURVIVAL IN SLOVENIA 1983–1997

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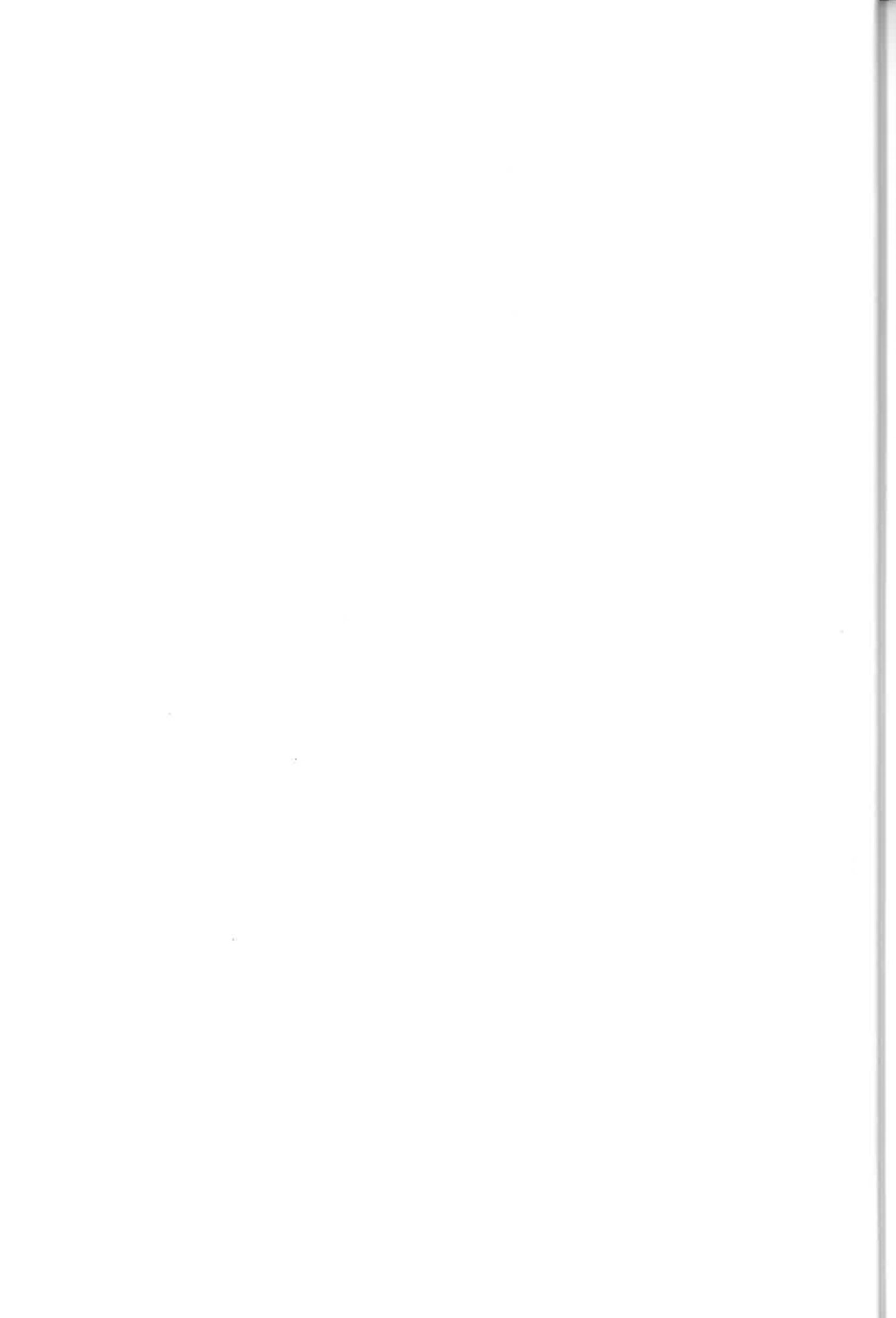
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ZAHVALA

Te knjige ne bi bilo brez vseh, ki so vestno prijavljali rakave bolezni od leta 1950 dalje in brez vztrajnega in natančnega dela vseh dosedanjih sodelavk Registra raka za Slovenijo.

ACKNOWLEDGMENT

This book would never have been published, had not it been for the persevering and conscientious work of all those who have been accurately reporting cancer cases in Slovenia since 1950, as well as of the whole staff of the Cancer Registry in Slovenia.



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PREGOVOR

Slovenci večkrat ne znamo dovolj ceniti svojih dosežkov. Tujci pogosto bolje vrednotijo naše delo in obstoj nekaterih naših ustanov. Mislim, da je tak primer tudi Register raka za Slovenijo in vse publikacije, ki jih skupina strokovnjakov te službe redno izdaja.

Redno objavljanje podatkov o incidenci različnih vrst raka in o preživetju bolnikov so dragoceno orodje nam, zdravnikom onkologom, za ocenjevanje uspešnosti našega zdravljenja v preteklosti in za načrtovanje zdravljenja v prihodnosti. Moralo pa bi biti nenehen vir podatkov tudi vsem tistim, ki načrtujejo in odločajo o vseh ukrepih boja proti raku, od preventivnih in presejalnih dejavnosti, do uvajanja novih načinov zdravljenja z dragimi zdravili. Nenezadnje bi morali biti podatki Registra tudi osnova za načrtovanje kadrovske politike na področju onkologije.

Podatki v tej knjigi odslukavajo pozornemu bralcu najrazličnejše vplive na rezultate zdravljenja. Če jih pravilno razumemo, bomo v prihodnje v boju z rakom lahko uspešnejši. Podatki kažejo, da smo pri preživetju bolnikov s tistimi raki, ki se večinoma zdravijo na Onkološkem inštitutu ali specializiranih oddelkih in klinikah Kliničnega centra (npr. rak ščitnice, maligni limfomi, sarkomi, germinalni tumorji) primerljivi z razvitimi državami Evrope. Slabši pa smo pri preživetju bolnikov s tistimi vrstami raka, ki se zdravijo v vseh bolnicah Slovenije. Ti rezultati kažejo, da je zdravljenje uspešnejše, če ga načrtuje in vodi specializirana multidisciplinarna skupina. Enako se je pokazalo v tujih študijah. Še veliko bomo morali postoriti za izobraževanje zdravnikov in za tesnejšo povezanost med Onkološkim inštitutom, Kliničnim centrom in ostalimi bolnišnicami, za tesnejše sodelovanje med razširjenim strokovnim kolegijem za onkologijo in kolegiji drugih strok in za primerno ozaveščanje javnosti s pomočjo civilne družbe.

Onkologi smo ponosni na naš Register in smo veseli, da ga imamo. Brez podatkov, ki so nam jih sodelavci te službe vedno sproti pripravljene posredovati, si našega dela sploh ne znamo več predstavljati. Ponosni smo tudi zato, ker ga imamo že od davnega leta 1950 in ker pokriva celotno območje Republike Slovenije. Registri mnogih večjih in bogatejših držav pokrivajo le 2–50% območja. Samo 9 od 20 držav, ki sodelujejo v študiji EURO-CARE-3 se ponaša s 100% zajetjem svojih stalnih prebivalcev z registrom raka. Ponosni smo lahko, da je med njimi tudi Slovenija. Hvaležni smo vsem sodelavcem Registra, ki marljivo, natančno, a skoraj anonimno opravljajo svoje delo in so nam vedno pripravljene pomagati s podatki in svojim znanjem. Njihovo delo je tako vpeto v vse klinične študije in objave.

FOREWORD

Slovenians usually tend to underestimate our national achievements. People from abroad often have higher appreciation for our work as well as for the activity of our national institutions. I dare say this also holds true for the Cancer Registry of Slovenia and for the publications that are regularly issued by the group of experts working at the Registry.

Regular publication of the data on the incidence of different cancers and on survival is of supreme importance for us, the oncologists; it is a feedback that serves as a tool to assess the efficiency of treatment in the past and to formulate future treatment plans. These publications are intended to be renewable resources of data for all who are involved in treatment planning and decision-making in fighting cancer, *viz.* from prevention and screening programs to initiating new treatment modalities with expensive drugs. The data published by the Registry should eventually serve as the basis for human resource management in oncology.

For a careful reader, the data gathered in this book are a reflection of diverse factors influencing the treatment outcome. If we draw sensible conclusions from them, our fight against cancer will be more successful in the future. These data show that the survival of our patients with the cancers (e. g. thyroid cancer, malignant lymphomas, sarcomas, germ cell tumors) that are predominantly treated at health centers specialized in cancer treatment, such as the Institute of Oncology in Ljubljana or some of the departments and clinics of the University Medical Centre of Ljubljana, are comparable with the survival in the developed countries in Europe. On the other hand, the survival of the patients affected with the cancers that are treated also in other hospitals throughout Slovenia is lower than that in European countries. These results indicate that cancer treatment can be more effective if it is planned and carried out by a specialized multidisciplinary team. The studies performed in other countries have reached the same conclusion. We still need to concentrate our efforts in further training of our physicians in oncology, in establishing constant cooperation of the Institute of Oncology of Ljubljana with the University Medical Centre of Ljubljana, and the remaining hospitals in Slovenia, in fostering closer cooperation between Slovenian Board on Oncology and other medical experts boards, and in raising public awareness through non-governmental organizations.

Slovenian oncologists are very proud of our Registry and extremely happy that we have it. Can we imagine how our work would go on without the data concurrently available from the Registry? Moreover, we can be also proud of our Registry because we have it since the distant 1950s and because it covers the entire region of the Republic of Slovenia. It is worth mentioning that the registries of other bigger and more prosperous countries than Slovenia cover no more than 2–50% of the country region. Only 9 of 20 countries included in the EURO-CARE-3 study have cancer registries that cover 100% of the population and it is our great honor to be one of these 9 countries. We are grateful to the assiduous and careful employees at the Registry who are at any time ready to provide us with data and help us with their knowledge. Their share of work is thus automatically interwoven with each clinical study or publication.

Prof. Marija Auersperg, Senior Adviser

UVOD

Podatki o preživetju bolnikov so kompleksna ocena bremena raka v opazovani populaciji. Zrcalijo uspešnost vseh programov onkološkega varstva, od množičnega presejanja in zgodnjega odkrivanja, do zdravljenja, rehabilitacije in dolgotrajnega spremljanja zdravstvenega stanja bolnikov. Na prikazano preživetje bolnikov z rakom so vplivali številni dejavniki, ki so povezani tako z bolniki samimi: starost, spol, telesna zmogljivost in spremljajoče bolezni, kot z rakom: lokacija in razširjenost bolezni ob diagnozi, histološka vrsta, način zdravljenja. Slednji pa je močno odvisen tudi od organizacije in razpoložljivosti celotne zdravstvene službe.

Dobra oskrba in zdravljenje v eni bolnišnici sta lahko izboljšala preživetje tam zdravljenih bolnikov. Na pomembnejše izboljšanje populacijskega preživetja pa sta vplivala le, če sta bila dosegljiva večini bolnikov v Sloveniji.

Pričujoča knjiga je drugo obsežnejše poročilo o preživetju vseh registriranih bolnikov z rakom v Sloveniji. V njej so podatki o preživetju bolnikov, ki so zboleli za rakom v letih 1983–97. Prvo obsežnejše poročilo smo izdali leta 1995 s podatki za zbolele v letih 1963–90 (1). Tako kot v prvi, tudi v tej o podatkih razpravljajo zdravniki, ki zdravijo bolnike z rakom. Ti zdravniki so kirurgi, radioterapevti-onkologi, internisti-onkologi in pediatri. Službujejo na Onkološkem inštitutu ali na kliničnih oddelkih Kliničnega centra v Ljubljani (KC). V tej knjigi jih je več kot v prvi, ker smo uredniki želeli, da bi o prikazanih podatkih razmišljali povsod, kjer se prične specifično zdravljenje bolnikov.

Namen knjige je soočiti se z izsledki uspehov zdravljenja v desetletnem obdobju 1988–97, jih primerjati z že objavljenimi izsledki v prvi knjigi in predvsem z izsledki evropske raziskave EUROCARE-3, ki obravnava bolnike iz let 1990–94. V njej je sodelovalo 66 populacijskih registrov raka iz 20 držav; med njimi tudi Slovenija.

Naše dejansko mesto v Evropi nas včasih opogumi, včasih strezni, skoraj vedno pa nam nakaže pot, po kateri lahko končen izid zdravljenja bolnikov z rakom v Sloveniji še izboljšamo neglede na sicer stalno prisotne izboljšave zdravljenja (nova zdravila, večje možnosti podpornega zdravljenja).

Od izdaje naše prve knjige leta 1995 je minilo sedem let. V tem času so tudi nekateri populacijski registri objavili nove, dopolnjene knjige o preživetju bolnikov z rakom (2, 3, 4, 5, 6, 7). Najodmevnejši pa sta bili prav gotovo publikaciji z izsledki študij EUROCARE-1 in EUROCARE-2 o preživetju bolnikov z rakom v različnih državah in regijah v Evropi (8, 9, 10, 11). Tretja publikacija s podatki EUROCARE-3 je v tisku (12). O populacijskem preživetju bolnikov z rakom so zdaj začeli razpravljati tudi na evropskih in svetovnih kongresih klinikov. Ugotovili so, da je največje preživetje bolnikov v Evropi manjše kot preživetje v ZDA. O tem in o možnih vzrokih so bili napisani prvi članki in zastavljene nove študije (13, 14, 15). Sistem onkološkega zdravstvenega varstva so prav na podlagi izsledkov EUROCARE-1 in EUROCARE-2 v Veliki Britaniji temeljito prevetrili, tamkajšnji registri raka so dobili nove naloge (16).

INTRODUCTION

Country-wide cancer survival data collected by population-based cancer registries provide comprehensive and complex measure of cancer burden in the observed population, as well as an evaluation of the effectiveness of cancer patient care in the country. They reflect the impact of all measures in cancer control programs, from mass screening to treatment, follow-up and rehabilitation of cancer patients. The observed survival rates are influenced by many patient-related factors, e. g. age, gender, performance status, concomitant diseases, and cancer-related factors, such as stage, histology and treatment of cancer. The latter depends considerably on the organization and availability of comprehensive oncology health care services.

Efficient management and treatment in a hospital could well improve the survival of the patients treated there. A significant impact of both on the increase of the population survival in Slovenia could have been observed if they had been accessible to the majority of patients in the country.

The present publication is the second comprehensive report on the survival of all cancer patients registered in Slovenia. It contains the data on the survival of patients who were diagnosed with cancer in the years 1983–97. The first comprehensive report on cancer survival data covering the period 1963–90 was published in 1995 (1). In this publication, as was also the case in the first one, cancer data are discussed and explained by the clinicians who are actually involved in the treatment process. These are surgeons, radiation oncologists, medical oncologists and a pediatrician. Most of them are employed at the Institute of Oncology Ljubljana and some at the clinical departments of the University Medical Centre (UMC) of Ljubljana. More authors were invited to participate in this book than in the earlier one because the editors wish to draw the attention to the presented data of all clinicians who are involved in primary treatment of cancer patients.

The aim of this publication is to present an overall estimate of the treatment results obtained in the ten-year period 1988–97 and correlate them with the results published in the first report and in particular with those of the European study EUROCARE-3 that covers the period 1990–94. Among 66 population-based registries from 20 countries participating in this study was also the Cancer Registry of Slovenia. The place that Slovenia holds in Europe, as much as it is encouraging at times, often brings us back to reality, and always shows us the way that we should follow in order to improve the results of cancer patients treatment in Slovenia.

It has now been seven years since we published the first comprehensive report in 1995. In this period, a number of population-based registries published new, updated reports on the survival of cancer patients (2, 3, 4, 5, 6, 7). The reports on the results of EUROCARE-1 and EUROCARE-2 are undoubtedly the most influential publications on the survival of cancer patients in European countries and regions (8, 9, 10, 11). The third publication containing the data on EUROCARE-3 is now in print (12). Population survival of cancer patients has become a frequent subject matter discussed by the clinicians at the European and world congresses. A general conclusion

PODATKI IN METODE

REGISTRACIJA RAKA V SLOVENIJI

Register raka za Slovenijo (Register) je bil ustanovljen pri Onkološkem inštitutu v Ljubljani leta 1950 na pobudo in pod vodstvom profesorice dr. Božene Ravnihar kot posebna služba za zbiranje in obdelavo podatkov o incidenci raka in o preživetju bolnikov z rakom. Prijavljanje raka je od takrat dalje v Republiki Sloveniji obvezno, z zakonom predpisano (*Ur. l. SRS*, št. 10/50, št. 29/50, št. 14/65, št. 1/80, št. 45/82, št. 42/85, *Ur. l. RS*, št. 9/92 in št. 65/00).

Register zbira informacije o bolnikih in njihovi rakavi boleznini. Bolnike identificira s pomočjo enotne matične številke občana (EMŠO) in posebne registrske številke, ki jo dobi ob prvi prijavi. Vpogled v podatke o bolezni pa je možen samo s pomočjo te registrske številke.

Glavni viri podatkov so bolnišnice v Sloveniji. Zaenkrat pošiljajo podatke še na posebnem obrazcu Prijava rakave bolezni. Te podatke Register dopolnjuje s prijavi zasebnih ordinacij ter z zdravniškimi poročili o vzroku smrti in obdukcijskimi zapisniki, v katerih je omenjena diagnoza rak.

Podatki o bolezni na prijavi so: primarna lokacija, histološka vrsta, razširitev bolezni (klinična in patološka), način ugotovitve diagnoze ter način zdravljenja.

ŠIFRIRANJE PODATKOV

V Registru šifrirajo podatke posebej izurjene diplomirane in višje medicinske sestre pod nadzorom zdravnika.

Primarno lokacijo od leta 1996 dalje šifrirajo po 10. in po 8. reviziji Mednarodne klasifikacije bolezni (17, 18). Pred tem je bila v uporabi samo 8. revizija. Šifro 10. revizije so vsem primerom dodali avtomatsko kasneje. Zaradi primerljivosti s prvo knjigo smo tudi v tej prikazali podatke po 8. reviziji.

Histološko vrsto od leta 1983 dalje šifrirajo po veljavni Mednarodni klasifikaciji za Onkologijo (ICD-O) (19).

Šifriranje in opredelitev razširitve bolezni (stadijev) solidnih tumorjev praviloma sledi klasifikaciji TNM (20). Je poenostavljena opredelitev stadijev, ki jo uporablja veliko registrov raka v Evropi in Ameriki in upošteva vse preiskovalne metode, vključno operacijo; če bolnik ni bil predhodno zdravljen, pa tudi obdukcijo. V omejen stadij je razvrščena bolezen, kjer je tumor označen kot T1 in T2 (razen pri dojki, malignem melanomu in pri ščitnici, kjer so vključeni tudi tumorji T3, in materničnem vratu in telesu ter sarkomih, kjer so vključeni le tumorji T1) in pri kateri niso prizadete regionalne bezgavke in ni zasevkov v oddaljenih organih (NOM0). V stadiju regionalne razširitve je bolezen, kjer je tumor opredeljen kot T3 in T4 (razen v omenjenih izjemah) in/ali so prizadete tudi regionalne bezgavke (N1), zasevkov v oddaljenih organih pa ni (M0). V stadiju oddaljene razširitve pa je tista bolezen, pri kateri so zasevki že v oddaljenih bezgavkah ali organih (M1). Maligni limfomi so opredeljeni po klasifikaciji *Ann-Arbor*.

of these meetings is that the highest survival of cancer patients in Europe is worse than that in USA. The first articles dealing with the same problem and its potential cause have started to appear and also new studies have been initiated (13, 14, 15). In Great Britain, the whole oncology health care system was reorganized on the basis of the results of EURO-CARE-1 and EURO-CARE-2 and the cancer registries in the country were given new tasks (16).

DATA AND METHODS

CANCER REGISTRATION IN SLOVENIA

The Cancer Registry of Slovenia (Registry) was founded in 1950 at the Institute of Oncology in Ljubljana, on the initiative and under the leadership of Professor Božena Ravnihar, as a special service for collecting, processing and analyzing the data on cancer incidence and cancer patient survival. Since then, notification and follow-up of cancer patients has been compulsory in Slovenia (*Official Gazette of SRS*, No. 10/50, No. 29/50, No. 14/65, No. 1/80, No. 45/82, No. 42/85, and *Official Gazette of RS*, No. 9/92 and No. 65/00).

The Registry collects a range of patient- and cancer-related information; the patients are identified by their personal identification number (PIN) and by unique registration numbers that every patient is given on the first registration. The access to the data on the disease of the patient is possible only by the registration number.

The main data sources are notifications gathered from all hospitals in Slovenia. This information is completed by the notifications from private clinics, death certificates, which are traced back, and autopsy protocols stating cancer diagnosis.

The collected items regarding cancer are primary site, histology, stage, basis for diagnosis, and treatment modality.

DATA CODING

Data are coded by specially trained registered nurses under a physician's supervision.

Since 1996, primary cancer sites have been coded according to the 10th and 8th revised edition of International Classification of Diseases (17, 18). Earlier, only the 8th revision was used. Later on, the code of the 10th revision was automatically added to all cases. In order to maintain the comparability with the first edition, the data coded according to the 8th revision are also presented in this report.

Histologic types have been coded according to the International Classification for Oncology (ICD-O) since 1983 (19).

As a rule, the coding and staging of solid tumors follow TNM classification (20). This is a simplified categorization of tumor stages that is applied by a great deal of cancer registries in Europe and the USA. It takes account of all diagnostic methods, including surgery and autopsy in cases when the patient has not been previously treated. Localized stage is defined by tumors of stages T1 and T2 (with the exception of breast

KAKOVOST PODATKOV IN POPOLNOST REGISTRACIJE

Kakovost podatkov Registra merita dva kazalca: odstotek primerov, ugotovljenih samo na osnovi zdravniških poročil o vzroku smrti in odstotek histološko potrjenih primerov raka. Popolnost registracije ugotavljamo posredno z razmerjem med umrljivostjo za rakom in incidenco ter ustaljenostjo incidence. Tabele 1–4 prikazujejo te kazalce v gradivu Registra v treh opazovanih obdobjih od 1983–97.

Kakovost podatkov se je izboljševala z napredkom diagnostičnih postopkov v slovenskem zdravstvu, z izobraževanjem osebja Registra in z večjimi možnostmi računalniške kontrole.

Popolnost registracije se je izboljševala postopno. Največ so k rednejšemu in popolnejšemu prijavljanju pripomogli kliniki sami, ko so želeli zvedeti za preživetje svojih bolnikov. Register jih je k temu spodbujal s povratno informacijo v okviru rednih letnih poročil, s prispevki v slovenski zdravstveni literaturi, na strokovnih srečanjih in s podatki o preživetju bolnikov, ki so bili zdravljeni pri njih. Zdravniška poročila o vzroku smrti so tudi eden od pomembnih dodatnih virov informacij že od leta 1950. Brez njih bi Register v letu 1997 izgubil podatke o 10% bolnikov, seveda samo tistih, pri katerih se je bolezen zaključila s smrtjo. Težko pa je ujeti tiste bolnike, ki so se zdravili samo ambulantno zaradi manj usodnih rakavih bolezni. Tako verjetno registracija nemelanomskih kožnih rakov ni popolna, ker jih splošne kirurške ambulante Regstru ne prijavljajo redno. Prav tako še vedno nekatere bolnišnice redno ne prijavljajo multiple-

Tabela 1: Število vseh novih primerov raka in odstotek registriranih samo na osnovi zdravniških poročil o vzroku smrti po spolu in obdobjih opazovanja. Slovenija 1983–97.

Table 1: Total number and percentage of new cancer cases registered from death certificates only by sex and period of observation. Slovenia 1983–97.

Obdobje Period	Št. novih primerov No. of new cases			% registracije samo na osnovi zdravniških poročil o vzroku smrti % of cases registered from death certificates only		
	Moški Males	Ženske Females	Vsi All	Moški Males	Ženske Females	Vsi All
1983–87	14468	13727	28195	3	3	3
1988–92	16733	15917	32650	4	4	4
1993–97	19628	19061	38689	3	3	3

Tabela 3: Število umrlih zaradi raka, število novih primerov raka ter količnik umrljivosti in incidence po obdobjih opazovanja. Slovenija 1983–97.

Table 3: Total number of deaths from cancer, number of new cancer cases, and the mortality/incidence ratio by periods of observation. Slovenia 1983–97.

Obdobje Period	Št. umrlih No. of deaths	Št. novih primerov No. of new cases	Umrljivost/Incidenca Mortality/Incidence
1983–87	19283	28195	0,68
1988–92	20795	32650	0,64
1993–97	27778	38689	0,72

tumors, malignant melanomas and thyroid carcinomas that also include T3 tumors, and of carcinomas of the uterine cervix, corpus and sarcomas that include only T1 tumors) without the involvement of regional lymph nodes and with no distant metastases (NOM0). Regional stage is defined by T3 and T4 tumors (except in the above mentioned cases) and/or with the involvement of regional lymph nodes (N1) but without distant metastases (M0). The distant stage of the disease is defined by metastatic spread into distant lymph nodes or other organs (M1). Malignant lymphomas are staged according to *Ann-Arbor* classification.

DATA QUALITY AND COMPLETENESS OF REGISTRATION

Data quality of a cancer registry is measured by two indicators: the percentage of cases for which registration was based on death certificates only, and the percentage of histologically verified cases; completeness of registration could be assessed by cancer incidence/mortality ratio and by the stability of incidence rates. The trends of these indicators in Slovenia are shown in Tables 1–4 for three observation periods from 1983 to 1997.

Data quality has been gradually improving during the study period along with advanced diagnostic procedures in Slovenia, with education of the Registry staff and greater possibilities for computerized internal consistency checks.

The completeness of registration has also been gradually improving. Clinicians themselves have contributed a great deal to regular and complete reporting because they were inter-

Tabela 2: Število vseh novih primerov raka* in odstotek mikroskopsko potrjenih po spolu in obdobjih opazovanja. Slovenija 1983–97.

Table 2: Total number of new cancer cases* and percentage of microscopically confirmed cases by sex and period of observation. Slovenia 1983–97.

Obdobje Period	Število Number			Odstotek Percentage		
	Moški Males	Ženske Females	Vsi All	Moški Males	Ženske Females	Vsi All
1983–87	14007	13274	27281	88	90	89
1988–92	16111	15234	31345	91	92	91
1993–97	19095	18521	37616	92	93	92

* Primeri, registrirani samo na osnovi zdravniških poročil o vzroku smrti, so izključeni.

* Cases, registered from death certificates only are excluded.

Tabela 4: Število vseh novih primerov raka, navedeno v letnih poročilih, in število ter odstotek naknadno prijavljenih po stanju z dne 15. 9. 2002 po obdobjih opazovanja. Slovenija 1983–97.

Table 4: Total number of new cancer cases, as cited in annual reports, and number and percentage of cases registered subsequently as on September 15, 2002 by periods of observation. Slovenia 1983–97.

Obdobje Period	Letna poročila Annual report	Naknadno prijavljeni Subsequently registered	Odstotek Percentage
	Število Number	Število Number	
1983–87	27316	879	3,2
1988–92	31835	815	2,6
1993–97	37341	1348	3,6

ga mieloma in kronične limfocitne levkemije v primeru, da so bolniki zdravljeni le ambulantno.

IZBOR BOLNIKOV

Populacijski register raka mora omejiti analizo preživetja na bolnike z območja, ki ga kot register pokriva. Bolniki, ki prihajajo na zdravljenje od drugod, so neznatna podskupina bolnikov z drugačnim pričakovanim trajanjem življenja.

Tako smo v analizo vključili samo bolnike s stalnim prebivališčem v Republiki Sloveniji, pri katerih je bil rak ugotovljen v obdobju 1983–97. Zaradi uporabljenega metodološkega pristopa smo bolnike, ki so bili izgubljeni iz opazovanja, vključili v analizo. Upoštevali smo tudi bolnike, ki so zboleli za več kot enim primarnim rakom. Število in odstotek teh bolnikov sta prikazana v tabeli 5. Njihovo število je s časom naraščalo, kar je posledica izboljšanih diagnostičnih možnosti, daljšega preživetja bolnikov kakor tudi popolnejše registracije.

Izključili pa smo bolnike, pri katerih rak ni bil ugotovljen za časa življenja. To so bolniki, ki so bili registrirani samo na osnovi zdravniških poročil o vzroku smrti ali pa je bil pri njih ugotovljen rak pri obdukciji. Pri obeh primerih je namreč datum diagnoze enak datumu smrti.

Podatke smo obdelali za vsako od 28. izbranih primarnih lokacij in za vse lokacije skupaj. Bolnike smo razdelili v starostne skupine: 0–14 let, 15–44 let, 45–54 let, 55–64 let, 65–74 let, 75 in več let. Ker je bilo pri otrocih, starih 0–14 let, število bolnikov majhno, smo posebj obravnavali le otroke z akutno levkemijo.

Obdelavo podatkov smo razslojili na tri opazovana obdobja (1983–87, 1988–92, 1993–97). Vitalno stanje bolnikov smo spremljali do 31. 12. 2001; tako smo večino bolnikov spremljali vsaj pet let.

SPREMLJANJE BOLNIKOV

Redno letno spremljanje vitalnega stanja vseh registriranih bolnikov poteka od ustanovitve Registra leta 1950. Tehnologija spremljanja se je spreminjala. Spremembe do leta 1990 smo podrobno opisali v prvi knjigi (1).

Za Register najpomembnejša sprememba se je dogodila leta 1990, ko smo podatkovno bazo dopolnili z manjkajočimi EMŠO. Od tedaj teče redno vsaj enkrat letno povezovanje s Centralnim registrom prebivalstva Slovenije in v bazo Registra se avtomatsko dodajajo podatki o smrti ali o tem, da je bolnik izgubljen iz opazovanja, npr. zaradi odselitve v drugo državo. V tem procesu povezovanja Register dosledno spoštuje določila Zakona o varstvu osebnih podatkov.

EMŠO, računalniško povezovanje in obnavljanje informacije o vitalnem stanju bolnikov so pripomogli k temu, da je izgubljenih iz opazovanja po petih letih manj kot pol odstotka in praktično onemogočili možnost dvojne registracije istega bolnika.

ested to get the data on the survival of their own patients. The Registry was additionally promoting clinicians' interest for regular reporting through the release of feed-back information in medical literature, regular annual reports and presentations at different workshops, and of the data on the survival of their own cancer patient series. Death certificates were one of the important data sources since 1950. In 1997, for example, the Registry would have lost the data on 10% of the cases, of course, only of fatal ones, if death certificates had not been provided. It is difficult to detect the patients with prognostically more favorable disease who were treated only in outpatient departments. The registration of non-melanoma skin cancer is most probably incomplete because of underreporting of general surgical outpatient departments. The registration of multiple myeloma and chronic lymphatic leukemia is also not complete because some hospitals do not regularly notify the cases that are managed in outpatient departments.

PATIENTS SELECTION

A population-based cancer registry should confine the analysis of survival to residents of the registry area since the patients migrating into the area for treatment only, will probably be an atypical subgroup with a rather different survival expectation.

Thus, only cancer patients, residents of Slovenia, diagnosed in the time period 1983–97 were included in the study. The lost to follow-up patients were included, and also the patients with more than one primary site. Registration and percentage of more than one primary cancer in the same individual is shown in Table 5. The increasing proportion of such patients is due to the improvements in diagnosis, survival and registration practice.

Cases registered exclusively from death certificates were excluded, as well as cases diagnosed at autopsy. In both, the dates of diagnosis and of death are the same.

All cancer sites together and 28 most frequent primary sites were analyzed. The age groups studied were: 0–14, 15–44, 45–54, 55–64, 65–74, and over 75 years. For children aged 0–14 years, only the data for acute lymphoblastic leukemia is presented and commented upon due to small number of cases.

The analyses were stratified by three five-year periods: 1983–87, 1988–92, and 1993–97. Patients were followed till December 31, 2001, so that the majority of patients were followed at least five years.

FOLLOW-UP OF PATIENTS

Follow-up of the vital status of the registered cancer patients has been performed annually since 1950. Methodology of the follow-up changed several times. The changes until 1990 were described in detail in the first comprehensive report (1).

A major change occurred in 1990 when the Registry's data base was updated with the personal identification numbers (PIN) and, from that year on, all registered patients are linked auto-

Tabela 5: Število vseh in število ter odstotek drugih in naslednjih primarnih rakov po obdobjih opazovanja. Slovenija 1963–97.

Table 5: Total number of new cancer cases and number and percentage of second and subsequent primary cancers by periods of observation. Slovenia 1963–97.

Obdobje Period	Vsi All			Dva primarna raka Two primary cancers		Trije primarni raki Three primary cancers		Štirje ali več primarnih rakov Four and more primary cancers	
	Število Number	Število Number	Odstotek Percentage	Število Number	Odstotek Percentage	Število Number	Odstotek Percentage	Število Number	Odstotek Percentage
1963–67	17827	315	1,8	11	0,1				
1968–72	19960	550	2,8	31	0,2	2	0,01		
1973–77	23093	846	3,7	31	0,1	2	0,01		
1978–82	25655	1320	5,2	61	0,2	1	0,00		
1983–87	28197	1620	5,8	86	0,3	2	0,00		
1988–92	32650	2118	6,5	131	0,4	6	0,02		
1993–97	38689	3054	7,9	227	0,6	16	0,04		

METODE

Preživetje bolnikov ocenjujemo z odstotkom bolnikov, ki so po izbranem časovnem obdobju od ugotovitve diagnoze še živi. Preživetje bolnikov z rakom običajno opazujemo po enem, treh in petih letih po diagnozi.

Možnosti in metod izračunavanja preživetja je več. Populacijski registri raka običajno izračunavajo opazovane in relativne odstotke preživetja in pri tem upoštevajo tudi krnjene bolnike (bolnike, ki so se izgubili iz opazovanja, zaradi preselitve izven območja registra ali zaradi tega, ker je bila dejanska doba opazovanja krajša).

Opazovani odstotek preživetja upošteva vse vzroke smrti in je odraz dejanske umrljivosti v opazovani skupini bolnikov. Vzroki smrti v posameznih skupinah bolnikov pa so različni, odvisni od lokacije raka ter starosti, spola in socialno-ekonomskega položaja bolnikov.

Relativni odstotek preživetja upošteva te razlike in je približek preživetja bolnikov v primeru, da bi upoštevali kot vzrok smrti samo proučevanega raka. Je količnik med dejansko opazovanim odstotkom preživetja in odstotkom preživetja, ki bi ga glede na spol in starost v opazovanem obdobju pričakovali v Sloveniji (pričakovano preživetje). Pričakovano preživetje smo izračunali iz tablic umrljivosti za Slovenijo (21, 22, 23).

Pričakovano preživetje se s starostjo manjša. Zato ima pri izračunu relativnega preživetja večji vpliv na starejše bolnike kot na mlajše. Razlika med opazovanim in relativnim preživetjem je zato pri starejših (npr. bolniki z rakom prostate) večja kot pri mlajših (npr. bolniki z rakom mod) (sliki 1 in 2).

Zaradi primerljivosti s prvo knjigo smo tudi v tej za izračun opazovanega, pričakovanega in relativnega preživetja uporabili računalniški program Hakulinena in sodelavcev (24). Program temelji na metodi življenjskih tablic, ki so jo v 50. letih opisali Berkson in Gage ter Cutler in Ederer. Ta metoda upošteva vse podatke do zaključka opazovanja, za krnjene bolnike pa predpostavlja, do so bili izpostavljeni verjetnosti smrti le polovico leta, v katerem smo jih prenehali opazovati.

V študiji EURO CARE-3 je relativno preživetje še starostno standardizirano. Starostna standardizacija je bila potrebna, ker je

matematično to Central Population Registry of Slovenia at least once a year, and death, as well as lost to follow-up events (e. g. emigration) are automatically added to the matricular part of the Registry's data base. During the linkage procedures, data protection laws are strictly respected.

PIN, computer linkage and updating of the vital status of all registered patients reduced the percentage of lost to follow-up patients after five-year observation period to a less than half per cent and also the possibility of a duplicate registration of the same person.

METHODOLOGY

Survival rates are based on proportions of patients alive at various times after diagnosis. Usually we are interested in the rates at fixed intervals of time after diagnosis, e. g. one, three and five years.

There are several options and methods for the calculation of survival rates. Population-based cancer registries usually use methods for the calculation of observed survival rates and relative survival rates, taking into account also the patients who have been lost to follow-up due to their emigration from the registry area or due to a shorter observation period.

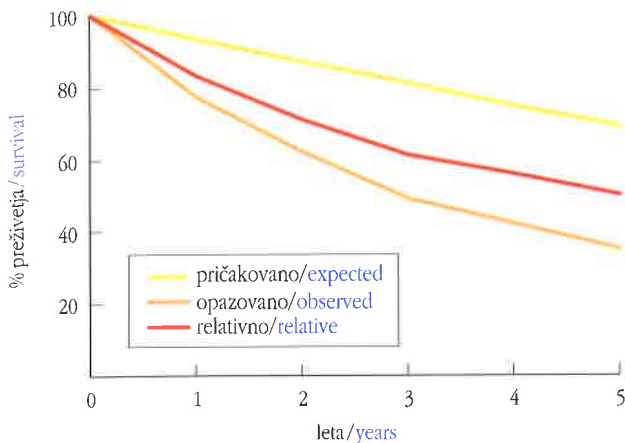
The observed survival rate accounts for all deaths, and is a true reflection of actual mortality in a patient group. The causes of death other than cancer may differ from group to group and depend on cancer site and patients' age, sex and socio-economic status.

The relative survival rate takes into account the above differences. It can be thought of as a probability of survival from cancer in the absence of other causes of death. The relative survival rate is the ratio of the observed actual survival rate and the survival rate that is, in the observation period, expected in general population of Slovenia with respect to sex and age (expected survival). In our analyses, the expected survival was calculated from Slovenian life tables (21, 22, 23).

The expected survival rate decreases with age; therefore, it has a stronger impact on the calculation of the relative survival rate of elderly patients than on that of young patients. Accordingly, the difference between the observed and relative survival is higher in elderly patients (e. g. patients with prostate carcinoma) than in young patients (e. g. patients with testicular carcinoma) (Figures 1, 2).

In order to maintain the comparability with our first comprehensive report, the computer package of Hakulinen et al. was applied for the calculation of the observed, expected and relative survival rates (24). This package is based on the actuarial, or life table method, which was described by Berkson and Gage and by Cutler and Ederer in the 50's. This method provides a means for using all the follow-up information accumulated up to the closing date of the observation period. The lost-to-follow-up patients are assumed to have been observed, on the average for one-half of the year during which they were withdrawn.

In the EURO CARE-3 study, the relative survival rate is also age-adjusted. The age-adjustment was indispensable because the age distribution of all patients included into the study varies from country to country. Age-adjusted survival rates are computed



SLIKA 1: Opazovano in pričakovano preživetje bolnikov z rakom prostate v Sloveniji 1993–97.

FIGURE 1: Observed and expected survival of prostate cancer patients in Slovenia 1993–97.

starostna porazdelitev v študijo vključenih bolnikov, med posameznimi državami različna. Uporabili so metodo direktne standardizacije. Kot standard so za vsako rakavo bolezen uporabili število primerov iz celotne podatkovne baze porazdeljene v petletne starostne razrede. Kot vsaka standardizacija pa tudi ta na nek način pači izsledke. Opazovano preživetje moških z želodčnim rakom v Sloveniji v letih 1990–94 je bilo 13%, relativno 17%, starostno standardizirano relativno pa 15%. Opazovano preživetje bolnikov z rakom mod je bilo 92%, relativno 94%, starostno standardizirano pa 93%. Odstopanja navzdol za slovenske podatke so večja pri moških kot pri ženskah.

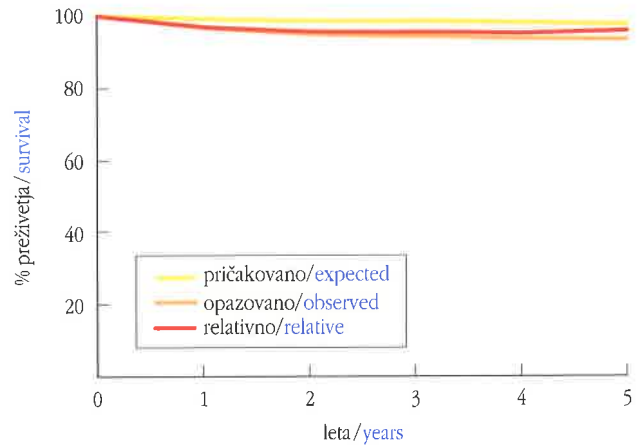
NAČIN PREDSTAVITVE PODATKOV

Preživetje bolnikov z rakom v Sloveniji opisujemo in o njem razpravljamo v 29 poglavjih. V posamezno poglavje so zajeti bolniki glede na organ, ki ga je rak prizadel npr. ustna votlina, dojka, pljuča. V zadnjem 29. poglavju opisujemo preživetje za vse bolnike z rakom skupaj, vključno s tistimi, ki zaradi redkega pojavljanja ali zaradi znano dobre prognoze (bolniki z nemelanomskim kožnim rakom) niso posebej obravnavani.

V uvodnem besedilu vsakega poglavja navajamo število v analizo vključenih in izključenih bolnikov, trend incidence obravnavane rakave bolezni, kakovost podatkov, odstotek posameznih histoloških vrst, načine zdravljenja in bolnišnice, v katerih se je prvo proti raku usmerjeno zdravljenje pričelo.

Na sliki 1 prikazujemo eno do petletno relativno preživetje bolnikov v zadnjih treh petletnih obdobjih opazovanja (1983–87, 1988–92, 1993–97) za oba spola skupaj. Podrobni podatki opazovanega in relativnega ena, tri in petletnega preživetja s 95% intervalom zaupanja glede na spol pa so navedeni v tabeli 3. Tabela 3 je primerljiva s tabelo 3 v našem prvem obsežnejšem poročilu (1).

Na sliki 2 prikazujemo za solidne rake podatke petletnega relativnega preživetja v zadnjih petih petletnih obdobjih opazovanja (1973–77, 1978–82, 1983–87, 1988–92, 1993–97) glede



SLIKA 2: Opazovano in pričakovano preživetje bolnikov z rakom mod v Sloveniji 1993–97.

FIGURE 2: Observed and expected survival of testicular cancer patients in Slovenia 1993–97.

by the direct method, using five age classes and the crude distribution of cases from the whole EURO-CARE-3 data base, for any given site, as standard. Regrettably, as any other age-adjustment also this one somehow distorts the results. The observed survival rate in Slovenian male patients with stomach cancer in the years 1990–94 was 13%, their relative survival rate was 17%, whereas their relative age-adjusted survival rate was 15%. The observed survival rate of patients with testicular cancer was 92%, relative 94% and relative age-adjusted 93%. Downward deviations of the data for Slovenia are greater in males than in females.

DATA PRESENTATION

The cancer patients' survival in Slovenia is described and discussed in 29 chapters. Each individual chapter deals with the survival of patients with respect to the site affected by cancer, e. g. oral cavity, breast, lung. In the last chapter, the survival for all cancer patients together, including those with rare cancers and those with non-melanoma skin cancer, is presented.

In the introduction of each chapter, the following data are presented: the number of patients included in the analysis, the number of excluded patients, incidence trend of the observed cancer site, data quality, percentage of individual histologic types, treatment modalities and hospitals in which the primary cancer treatment was started.

Figure 1 in each chapter shows one- to five-year relative survival for patients of both sexes together in the three recent five-year observation periods (1983–87, 1988–92, 1993–1997). Detailed data (95% confidence interval) on the observed and relative one-, three-, and five-year survival by sex are presented in Table 3. Table 3 in this report is comparable with the Table 3 published in our first comprehensive report (1).

Figure 2 presents the data on five-year relative survival in the five recent five-year observation periods (1973–77, 1978–82, 1983–87, 1988–92, 1993–97) with respect to the disease stage. The exact number and percentage of the cancer patients as to the stage of the disease are given in Table 2 that is comparable

na razširjenost bolezni (stadij). Število in odstotek bolnikov glede na stadij sta navedena v tabeli 2. Tudi ta tabela je primerljiva s tabelo 2 v prvem poročilu (1). Način opredeljevanja razširjenosti bolezni v Registru je podrobno opisan v poglavju Šifriranje podatkov. Za vse rake skupaj in za krvne rakave bolezni pa so na tej sliki prikazane spremembe v preživetju glede na starost bolnikov.

Na sliki 3 prikazujemo relativno eno do petletno preživetje za zadnje petletno obdobje (1993–97) glede na starost. V tem prikazu so izpuščene starostne skupine z manj kot 10 primeri, pri posameznih manj pogostnih rakavih boleznih so v prikazu podatki za oba spola združeni. Podrobni podatki o številu bolnikov po posameznih starostnih skupinah so navedeni v tabeli 1.

Pri nekaterih manj pogostnih boleznih se pri najstarejši skupini krivulja relativnega preživetja po treh letih opazovanja obrne navzgor. To si razlagamo s tem, da so preživeli bolniki imeli boljše preživetje, kot bi ga glede na njihovo starost pričakovali. V nekem smislu so izbrana skupina ljudi, ki je bila zaradi svoje osnovne bolezni v večji meri zdravstveno nadzorovana, kot enako stara splošna populacija Slovenije (25).

Naštetim slikam in tabelam sledi primerjava starostno standardiziranega relativnega petletnega preživetja bolnikov v Sloveniji z analizo preživetja 66 registrov raka iz 20 držav Evrope v letih 1990–94, vključenih v študijo EUROCORE-3 (12).

Sledi razpravljanje klinikov različnih specialnosti, ki se že vrsto let ukvarjajo z zdravljenjem v poglavju obravnavane rakave bolezni. Razpravljajo o tistih spremembah v diagnostiki in zdravljenju, ki so v zadnjem desetletnem obdobju opazovana lahko vplivale na preživetje bolnikov z rakom v Sloveniji.

with the Table 2 published in our first comprehensive report (1). The methodology for the disease staging is explained in details in the chapter Data Coding. For all cancer sites and leukemias, the changes in survival are, in this figure, presented by age.

Figure 3 shows relative one- to five-year survival rates in the last five-year observation period (1993–97) with respect to the patients' age. This presentation does not include the age groups with less than 10 patients. In some rare cancers, the survival data for both sexes are presented together. The detailed data on the number of patients in particular age group of patients are given in Table 1.

In some rare cancers, the relative survival curve of the oldest age groups starts to rise after a three-year observation period. This indicates that, with respect to their age, these patients survived better than expected. In a sense, cancer patients are, due to the nature of their disease, a selected group of patients that have a better access to health care services as the rest of the population of the same age (25).

After the figures and tables, each chapter makes a comparison of the age-adjusted relative five-year survival of cancer patients in Slovenia for the period 1990–94 with the average age-adjusted survival rate obtained from 66 registries of 20 European countries (EUROCORE-3) (12).

The presented data and tables are then discussed by clinicians of different medical specialties and with many years' experience in the treatment of the cancer that is dealt with in the chapter. They comment the changes that occurred in the diagnostics and treatment of cancer in the last ten years that might have influenced the cancer patient's survival in Slovenia.

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VIRI

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IZSLEDKI IN RAZPRAVA

RESULTS AND DISCUSSION

USTNA VOTLINA

ORAL CAVITY

MKB 8/ICD 8: 1411–1419, 143, 144, 145

V obdobju 1983–97 je zbolelo za rakom v ustni votlini 1252 moških in 188 žensk, od tega v letih 1993–97 426 moških in 76 žensk. V analizo ni bilo vključenih 25 (2%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka ustne votline večala predvsem pri ženskah. V letih 1983–87 je bila groba incidenčna stopnja 8,7/100.000 moških in 1/100.000 žensk, v letih 1993–97 pa 8,9/100.000 moških in 1,5/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal z 98% v letih 1983–87 na 100% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 91% ploščatočeličnih karcinomov, 4% neopredeljenih karcinomov in 3% ne-Hodgkinovih limfomov.

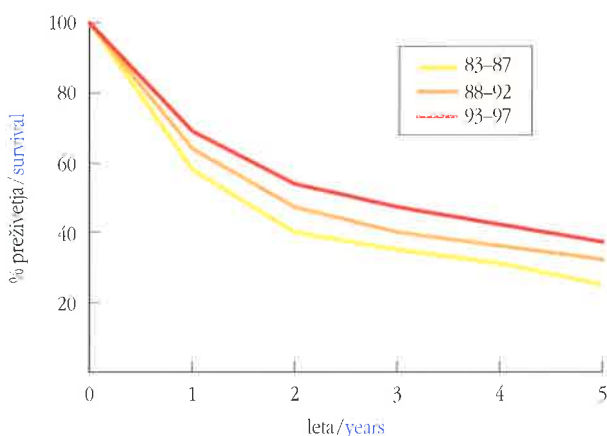
Starostna porazdelitev v analizo zajetih bolnikov se ni pomembno spremenila (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila. V zadnjem obdobju je bilo več bolnikov ugotovljenih z omejeno boleznijo (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 95% bolnikov. Prvo zdravljenje je bilo v 35% obsevalno, v 35% kirurško in obsevalno, v 21% samo kirurško in v 5% obsevalno in citostatsko. Z operacijo, obsevanjem in kemoterapijo je bil zdravljen 1% bolnikov. Prvo zdravljenje se je pričelo v 43% na

TABELA 1: Ustna votlina. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Oral cavity. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi/ Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	400	1	31	118	154	72	24
Males	1988-92	411	0	46	120	174	57	14
	1993-97	424	0	50	101	168	86	19
Ženske	1983-87	50	0	6	7	18	10	9
Females	1988-92	55	0	3	8	20	10	14
	1993-97	75	0	12	17	18	14	14



SLIKA 1: Relativno petletno preživetje bolnikov z rakom ustne votline, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of oral cavity cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 1,252 male and 188 female patients were diagnosed with tongue and mouth cancer; of these, 426 males and 76 females were diagnosed with this cancer in the five-year period 1993–97. In 25 patients (2%), oral cavity cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of oral cavity cancer increased in women. In 1983–87, the crude incidence rate was 8.7/100,000 in males and 1/100,000 in females, whereas in 1993–97, it was 8.9/100,000 in males and 1.5/100,000 in females. In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 2%, i. e. from 98% to 100%. In the years 1993–97, the percentage of squamous-cell carcinomas, non-specified carcinomas, and non-Hodgkin lymphomas in the microscopically confirmed cases was 91%, 4% and 3%, respectively.

The age distribution of the patients included into the analysis has not changed significantly (Table 1), whereas the stage distribution at diagnosis changed. In the last observation period, a higher percentage of patients with localized disease was observed (Table 2).

In the period 1993–97, 95% of patients underwent specific treatment. Radiotherapy was applied as primary treatment in

TABELA 2: Ustna votlina. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

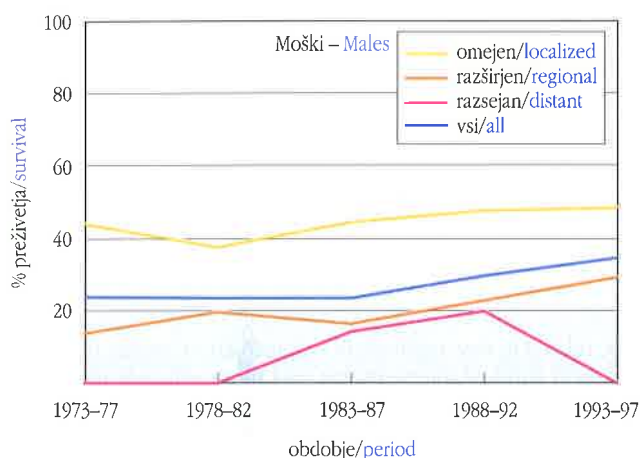
TABLE 2: Oral cavity. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij/Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsrejan/ Distant	Neznan/ Unknown	%			
Moški	1983-87	400	95	23,8	291	72,8	8	2,0	6	1,5
Males	1988-92	411	111	27,0	283	68,9	11	2,7	6	1,5
	1993-97	424	140	33,0	269	63,4	9	2,1	6	1,4
Ženske	1983-87	50	22	44,0	26	52,0	0	0,0	2	4,0
Females	1988-92	55	23	41,8	29	52,7	1	1,8	2	3,6
	1993-97	75	27	36,0	47	62,7	0	0,0	1	1,3

TABELA 3: Ustna votlina. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Oral cavity. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	55	(50-60)	31	(26-36)	20	(16-24)	68	(55-81)	44	(30-58)	34	(21-47)
1988-92	60	(55-65)	35	(30-40)	26	(22-30)	78	(67-89)	49	(35-63)	44	(31-57)
1993-97	64	(60-68)	40	(36-44)	30	(26-34)	84	(76-92)	60	(49-71)	47	(35-59)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	56	(51-61)	33	(28-38)	23	(18-28)	70	(57-83)	48	(33-63)	40	(24-56)
1988-92	62	(57-67)	38	(33-43)	30	(25-35)	80	(69-91)	54	(39-69)	51	(35-67)
1993-97	66	(61-71)	44	(39-49)	35	(30-40)	86	(78-94)	65	(53-77)	53	(39-67)



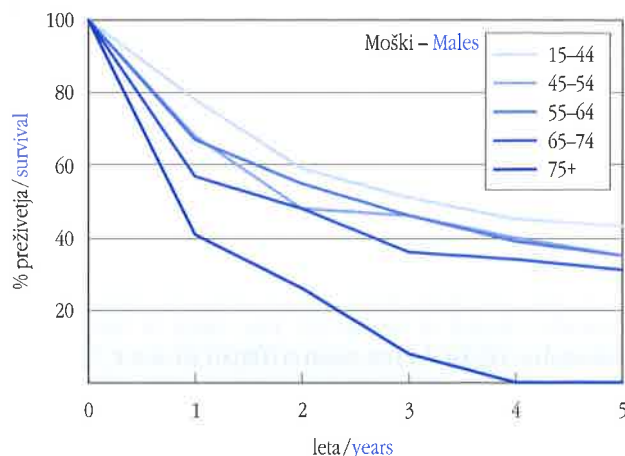
SLIKA 2: Relativno petletno preživetje bolnikov z rakom ustne votline, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.

FIGURE 2: Relative five-year survival of oral cavity cancer patients diagnosed in the period 1973–1997 by stage and period of diagnosis.

Onkološkem inštitutu v Ljubljani, v 25 % na Kliniki za otorinolaringologijo in cervikofacialno kirurgijo Kliničnega centra v Ljubljani (KC), v 21 % na Kliničnem oddelku za maksilofacialno kirurgijo KC, v 8 % v Splošni bolnišnici (SB) Maribor in po 1 % v SB Murska Sobota in v SB Šempeter pri Novi Gorici.

V letih 1993–97 je bilo relativno petletno preživetje za 12 % večje kot v letih 1983–87 (slika 1). Preživetje se je povečalo pri omejeni in razširjeni bolezni (slika 2). Preživetje je bilo pri starejših od 75 let za več kot 30 % manjše kot pri mlajših (slika 3).

V študiji EURO CARE-3 so posebej obravnavali jezik in posebej ostale dele ustne votline. Povprečno starostno standardizirano relativno petletno preživetje je bilo v Evropi za rak jezika 33,2 % (27,3–40,4) pri moških in 48,8 % (43,6–54,7) pri ženskah, v Sloveniji pa 25,1 % (18,6–33,9) pri moških in 41 % (25,8–65,2) pri ženskah. Največji odstotek pri moških je bil 50,9 na Nizozemskem (samo območji registrov Amsterdam in Eindhoven) in pri ženskah 80,1 na Tirolskem v Avstriji. Za raka



SLIKA 3: Relativno petletno preživetje bolnikov z rakom ustne votline, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of oral cavity cancer patients diagnosed in the period 1993–1997 by age.

35% of patients, in another 35% of patients, the primary treatment was surgery combined with radiotherapy, 21% of patients received surgery alone, 5% were treated with radio- and chemotherapy, and 1% with surgery, radio- and chemotherapy. Primary treatment started at the Institute of Oncology Ljubljana in 43%, at the Department of Otorhinolaryngology and Cervicofacial Surgery of the University Medical Centre in Ljubljana (UMC) in 25%, at the Department of Maxillofacial Surgery of UMC in 21%, in the General Hospital in Maribor 8%, and 1% each in the General Hospitals in Murska Sobota and Šempeter pri Novi Gorici.

The relative five-year survival rate was 12% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The survival increased in localized and regional disease (Figure 2). The survival was around 30% lower in the patients aged over 75 than in younger patients (Figure 3).

According to the EURO CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival

ustne votline pa je bilo povprečno starostno standardizirano relativno petletno preživetje pri moških v Evropi 39,9% (35,2–45,2), v Sloveniji pa 21,5 (16,6–27,8), največje pa 64,8% v Švici (samo območji registrov iz Basla in Ženeve).

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Pomembno večje preživetje bolnikov z rakom v ustni votlini v zadnjem obdobju gre na račun večjega odstotka bolnikov odkritih v zgodnejših stadijih bolezni in na račun večjega deleža ozdravljenih bolnikov z razširjeno boleznijo.

Ker presejalnih programov za bolnike s karcinomom v področju glave in vratu v Sloveniji ni, je najverjetneje k zgodnejšemu odkrivanju raka v ustni votlini, ki je enostavnemu pregledu najbolj dostopna, prispevala boljša zdravstvena ozaveščenost prebivalstva in večje znanje zdravnikov.

Razlogi za boljši izhod zdravljenja bolnikov z razširjenim karcinomom ustne votline so najverjetneje radikalnejši kirurški posegi, ki so jih omogočili novi načini rekonstrukcije ter ustreznejši način obsevanja.

Dodatno izboljšanje, ki je potrebno in možno, bo mogoče doseči z zgodnejšo detekcijo in izboljšanjem tehničnih in kadrovskih možnosti diagnostike in obsevanja, kar velja tudi za druge malignome v področju glave in vratu.

rate of the patients with tongue cancer was 33.2% (27.3–40.4) in male patients and in female patients 48.8% (43.6–54.7), while in Slovenia, it was 25.1% (18.6–33.9) in male patients and 41% (25.8–65.2) in female patients. The highest survival of 50.9% and of 80.1% was observed in male patients in the Netherlands (only in the regions of Amsterdam and Eindhoven) and in female patients in Tyrol in Austria. In Europe, the age-standardized relative survival rate of male patients with oral cancer was 39.9% (35.2–45.2), while in Slovenia it was 21.5% (16.6–27.8). The highest survival of 64.8% was observed in male patients in Switzerland (only registries from Basel and Geneva).

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The recent, significantly higher survival of the patients with tongue and mouth cancer is mainly due to higher percentages of early detected cases and a higher cure rate in patients with regionally advanced disease.

As there is no screening for the head and neck cancer, the detection of the mouth and tongue cancer in its early stages may be due to easy accessibility of clinical examination, to a growing awareness of cancer among the general population and expanded knowledge and skills of clinicians about it.

The reasons for a more favorable outcome of treatment of patients with the advanced mouth and tongue cancer could be related to new methods of reconstruction surgery that allow radical surgical interventions and more efficient irradiation regimes.

Further improvement in survival, which is as much imperative as feasible, could be achieved by earlier detection, updated technical equipment and advanced knowledge and skills of the personnel which should have been also taken into account in the treatment of other head and neck cancers.

ŽRELO

PHARYNX

MKB 8 / ICD 8: 1410, 146, 148

V obdobju 1983–97 je zbolelo za rakom žrela 1468 moških in 144 žensk, od tega v letih 1993–97 769 moških in 79 žensk. V analizo ni bilo vključenih 27 (1,7%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka žrela večala. V letih 1983–87 je bila groba incidenčna stopnja 13,3/100.000 moških in 1,2/100.000 žensk, v letih 1993–97 pa 16/100.000 moških in 1,5/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal s 97% v letih 1983–87 na 99% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 91% ploščatočeličnih karcinomov, 1% neopredeljenih karcinomov, 3 primeri žlezni karcinomov in 2 primera mukoepidermoidnega karcinoma. Ne-Hodgkinovih limfomov pa je bilo 7%.

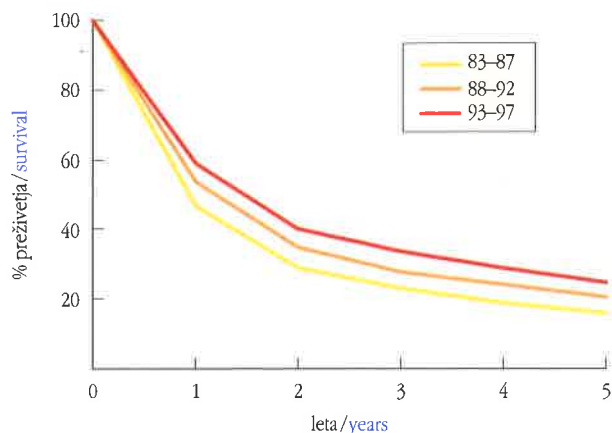
Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bil odstotek starejših od 55 let večji. Razširjenost bolezni ob diagnozi se je le malo spremenila. V zadnjem obdobju je bilo samo za 3% več bolnikov ugotovljenih z omejeno boleznijo (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 94% bolnikov. Prvo zdravljenje je bilo v 51% obsevalno, v 26% kirurško in obsevalno, v 16% obsevalno in citostatsko in le v 3% samo kirurško. Z operacijo, obsevanjem in kemoterapijo je bilo

TABELA 1: Žrelo. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Pharynx. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87 1988-92 1993-97	610 682 760	0 0 0	46 75 73	217 205 208	228 262 304	90 101 152	29 39 23
Ženske Females	1983-87 1988-92 1993-97	60 60 77	1 0 0	2 3 5	11 12 13	21 20 26	10 12 20	15 13 13



SLIKA 1: Relativno petletno preživetje bolnikov z rakom v žrelu, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of laryngeal cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 1,468 male and 144 female patients were diagnosed with pharyngeal cancer; of these, 769 males and 79 females were diagnosed with this cancer in the five-year period 1993–97. In 27 patients (1.7%), pharyngeal cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of pharyngeal cancer increased. In 1983–87, the crude incidence rate was 13.3/100,000 in males and 1.2/100,000 in females whereas in 1993–97, it was 16/100,000 in males and 1.5/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 2%, i. e. from 97% to 99%. In the years 1993–97, the percentage of squamous cell, non-differentiated cell carcinomas, non-Hodgkin lymphomas in the microscopically confirmed pharyngeal cancers was 91%, 1%, and 7%, respectively; 3 cases were adenocarcinomas and 2 mucoepidermoid carcinomas.

The age distribution of the patients included into the analysis has changed (Table 1). In the period 1993–97, the number of patients aged over 55 was higher. The stage distribution at diagnosis did not change considerably. In the last observation period, the percentage of localized disease increased by 3% (Table 2).

TABELA 2: Žrelo. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

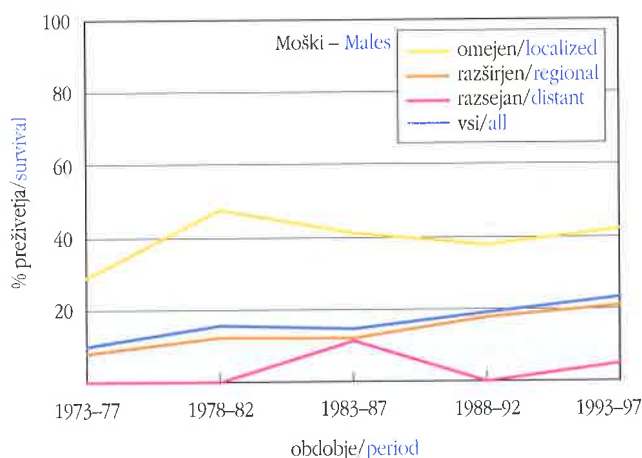
TABLE 2: Pharynx. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%				
Moški Males	1983-87 1988-92 1993-97	610 682 760	57 79 90	9,3 11,6 11,8	525 562 639	86,1 82,4 84,1	20 28 24	3,3 4,1 3,2	8 13 7	1,3 1,9 0,9
Ženske Females	1983-87 1988-92 1993-97	60 60 77	8 13 11	13,3 21,7 14,3	47 41 60	78,3 68,3 77,9	3 6 5	5,0 10,0 6,5	2 0 1	3,3 0,0 1,3

TABELA 3: Žrelo. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).**TABLE 3:** Pharynx. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years					Ženske / Females Leta / Years						
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983–87	45	(41–49)	19	(16–22)	13	(10–16)	57	(44–70)	40	(27–53)	25	(14–36)
1988–92	53	(49–57)	26	(23–29)	18	(15–21)	65	(53–77)	41	(28–54)	38	(25–51)
1993–97	57	(53–61)	30	(27–33)	20	(17–23)	65	(54–76)	51	(40–62)	39	(28–50)

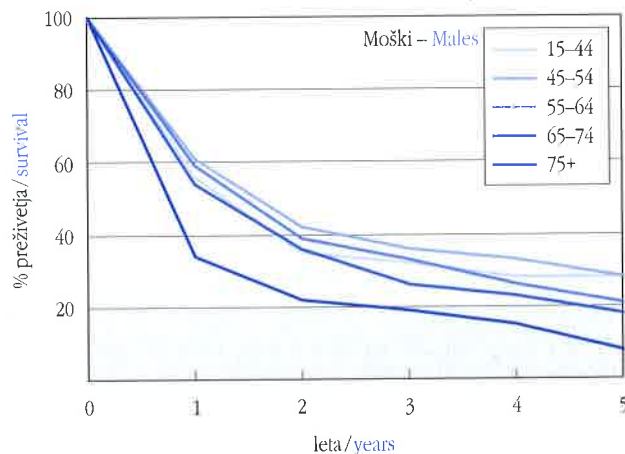
Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years					Ženske / Females Leta / Years						
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983–87	46	(42–50)	20	(17–23)	15	(12–18)	59	(46–72)	44	(30–58)	30	(17–43)
1988–92	53	(49–57)	26	(22–30)	19	(16–22)	67	(54–80)	45	(31–59)	44	(29–59)
1993–97	58	(54–62)	32	(28–36)	23	(20–26)	67	(56–78)	55	(43–67)	45	(32–58)

**SLIKA 2:** Relativno petletno preživetje bolnikov z rakom žrela, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.**FIGURE 2:** Relative five-year survival of pharyngeal cancer patients diagnosed in the period 1973–1997 by stage and period of diagnosis.

zdravljenih 2% bolnikov. Prvo zdravljenje se je pričelo v 68% na Onkološkem inštitutu v Ljubljani, v 20% na Kliniki za otorinolaringologijo in cervikofacialno kirurgijo KC, v 10% v SB Maribor.

V letih 1993–97 je bilo relativno petletno preživetje za 9% večje kot v letih 1983–87 (slika 1). Preživetje se je povečalo pri bolnikih z razširjeno boleznijo (slika 2). Preživetje je bilo pri starih 65–74 let za 10% manjše kot pri starih 45–54 let in za 10% večje kot pri starejših od 75 let (slika 3).

V študiji EURO-CARE-3 so posebej obravnavali ustno in spodnje žrelo. Povprečno starostno standardizirano relativno petletno preživetje pri raku ustnega žrela je bilo v Evropi 25,3% (21,8–29,3) pri moških in 41,9% (34,2–51,3) pri ženskah, v Sloveniji pa 15,1% (11,6–19,7) pri moških in 20,8% (14,4–30) pri ženskah. Največji odstotek pri moških in pri ženskah je bil na Nizozemskem (samo v območjih registrov Amsterdam in Eindhoven) 42,3% oziroma 59,1%. V Evropi je bilo povprečno starostno standardizirano relativno petletno preživetje za

**SLIKA 3:** Relativno petletno preživetje bolnikov z rakom žrela, zbolelih v letih 1993–1997 po starosti.**FIGURE 3:** Relative five-year survival of pharyngeal cancer patients diagnosed in the period 1993–1997 by age.

In the period 1993–97, 94% of patients underwent specific treatment; radiotherapy was applied as primary treatment in 51% of patients, in another 26% of patients, the primary treatment was surgery combined with radiotherapy, 16% received radio- and chemotherapy, only 3% were treated with surgery alone, and 2% underwent surgery, radio- and chemotherapy. Primary treatment was started at the Institute of Oncology Ljubljana in 68% of patients, at the Department of Otorhinolaryngology and Cervicofacial Surgery of UMC in Ljubljana in 20% of patients and in the General Hospital in Maribor in 10%.

The relative five-year survival rate was 9% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The survival increased in the patients with regional disease (Figure 2). In the patients aged 65–74 years, the survival was 10% lower than in patients aged 45–54, and 10% higher than in patients over 75 (Figure 3).

In the EURACARE-3 study the survival for oro- and hypopharyngeal cancer were presented separately. For the peri-

raka spodnjega žrela pri moških 21,3% (16,9–26,7), v Sloveniji pa pri moških 17,1% (11,8–24,7). Največje preživetje pri moških je bilo 31,6% na Norveškem.

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Kljub pomembnemu izboljšanju preživetja bolnikov s karcinomom žrela z izidi še ne moremo biti zadovoljni. Glede na to, da ni v nasprotju z ustno votlino praktično nobenega premika v razporeditvi stadijev na bolje, gre izboljšanje preživetja na račun zdravljenja. Izid zdravljenja pri omejeni bolezni se ni izboljšal, izboljšanje je bilo doseženo zgolj pri bolnikih z boleznijo v razširjenem stadiju. K temu izboljšanju je najverjetneje prispeval nov pristop zdravljenja s sočasno kombinacijo obsevanja in kemoterapije (1, 2).

VIRA

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2. Zakotnik B, Šmid L, Budihna M et al. Concomitant radiotherapy with mitomycin C and bleomycin compared with radiotherapy alone in inoperable head and neck cancer: final report. *Int J Radiat Oncol Biol Phys* 1998; 41: 1121–7.

od 1990–94, in Europe, the age-standardized relative survival rate of the patients with oropharyngeal cancer was 25.3% (21.8–29.3) in male patients and in female patients 41.9% (34.2–51.3), while in Slovenia, it was 15.1% (11.6–19.7) in male patients and 20.8% (14.4–30) in female patients. The highest survival of 42.3% and of 59.1% was observed in the Netherlands (only in the regions of Amsterdam and Eindhoven) in male and in female patients, respectively. In Europe, the age-standardized relative survival rate of the male patients with hypopharyngeal cancer in male was 21.3% in (16.9–26.7), while in Slovenia it was 17.1% (11.8–24.7). The highest survival of 31.6% was observed in male patients in Norway.

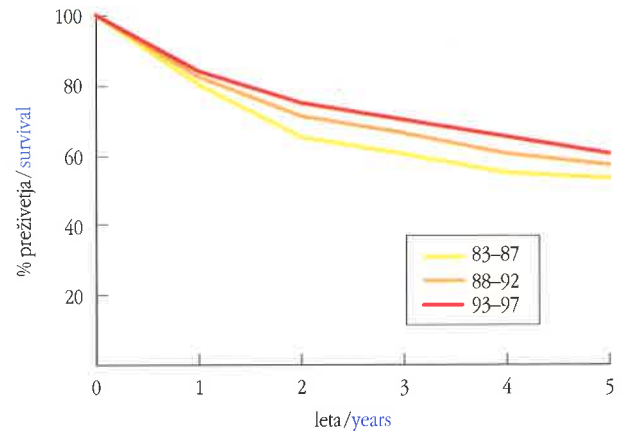
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Despite a significant improvement of the survival of patients with pharyngeal cancer, the treatment outcome has not yet reached a satisfactory level. In contrast to the observed progress of stage distribution of the disease in oral cavity, no improvement was observed in the pharyngeal cancer stage distribution. Better survival is therefore primarily due to better treatment regimes. The treatment outcome in localized disease did not improve, but an improvement was observed in the patients with regional disease. The reason for this improvement may simply lie in new treatment approaches, such as concomitant radio- and chemotherapy (1, 2).

GRLO

LARYNX

MKB 8/ICD 8: 161



SLIKA 1: Relativno petletno preživetje bolnikov z rakom grla, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of laryngeal cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom grla 1474 moških in 123 žensk, od tega v letih 1993–97 478 moških in 48 žensk. V analizo ni bilo vključenih 42 (3%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti. Med vključenimi je bilo v letih 1983–87 37% raka glasilk, v letih 1993–97 pa 41%.

V opazovanem 15-letnem obdobju se incidenca raka grla ni pomembno spremenila. V letih 1983–87 je bila groba incidenčna stopnja 10,2/100.000 moških in 0,7/100.000 žensk, v letih 1993–97 pa 9,9/100.000 moških in 0,9/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal s 97% v letih 1983–87 na 99% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 97% ploščatočeličnih karcinomov, 2% neopredeljenih karcinomov, 3 primeri verukoznega karcinoma, 2 primera žleznega karcinoma in po en primer ne-Hodgkinovega limfoma in leiomiosarkoma.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 se je povečalo število bolnikov, starih 65 let in več. Razširjenost bolezni ob diagnozi se je spremenila. V zadnjem obdobju je bilo ugotovljeno več bolezni z regionalno razširitvijo (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 96% bolnikov. Prvo zdravljenje je bilo v 53% obsevalno, v 35% kirurško in obsevalno, v 10% samo kirurško, v 2% obsevalno in citostat-

TABELA 1: Grlo. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Larynx. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	461	0	30	124	179	84	44
Males	1988-92	508	0	43	111	202	104	48
	1993-97	465	0	44	93	175	121	32
Ženske	1983-87	33	0	7	5	16	4	1
Females	1988-92	42	0	4	9	17	7	5
	1993-97	46	0	6	8	14	14	4

In the period 1983–97, a total of 1,474 male and 123 female patients were diagnosed with laryngeal cancer; of these patients, 478 males and 48 females were diagnosed with this cancer in the five-year period 1993–97. In 42 patients (3%), this cancer was diagnosed at death; these patients were therefore not included in the analysis. In the periods 1983–87 and 1993–97, the glottic cancer was diagnosed in respectively 37% and 41% of the patients included into the analysis.

In the observed 15-year period, the incidence of laryngeal cancer did not significantly change. In 1983–87, the crude incidence rate was 10.2/100,000 in males and 0.7/100,000 in females, whereas in 1993–97, it was 9.9/100,000 in males and 0.9/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the period 1993–97 was 2%, i. e. from 97% to 99%. In the years 1993–97, the percentage of squamous cell and non-differentiated cell carcinomas in the microscopically confirmed laryngeal cancers was 97% and 2%, respectively; in addition, 3 cases were verrucous carcinoma, 2 cases were adenocarcinoma, 1 non-Hodgkin lymphoma and 1 leiomiosarcoma.

The age distribution of the patients included into the analysis has changed (Table 1). In the period 1993–97, the num-

TABELA 2: Grlo. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

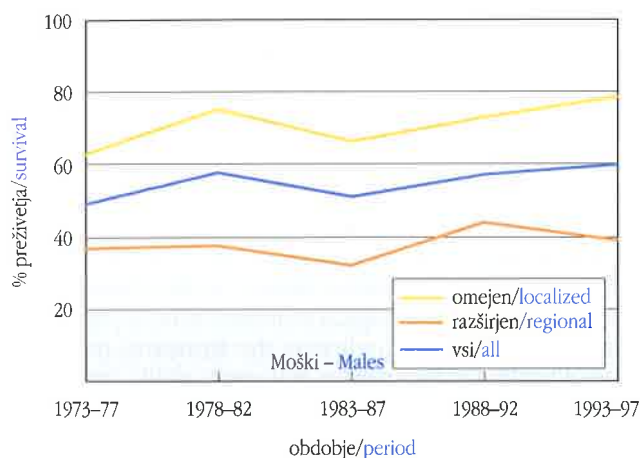
TABLE 2: Larynx. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij/Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%			
Moški	1983-87	461	261	56,6	183	39,7	3	0,7	14	3,0
Males	1988-92	508	244	48,0	248	48,8	6	1,2	10	2,0
	1993-97	465	254	54,6	206	44,3	5	1,1	0	0,0
Ženske	1983-87	33	18	54,5	15	45,5	0	0,0	0	0,0
Females	1988-92	42	20	47,6	22	52,4	0	0,0	0	0,0
	1993-97	46	28	60,9	17	37,0	0	0,0	1	2,2

TABELA 3: Grlo. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Larynx. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	77	(73-81)	53	(48-58)	43	(38-48)	88	(77-99)	73	(57-89)	69	(53-85)
1988-92	80	(76-84)	60	(56-64)	49	(45-53)	69	(55-83)	62	(47-77)	55	(40-70)
1993-97	82	(78-86)	63	(59-67)	51	(46-56)	85	(74-96)	70	(56-84)	59	(44-74)

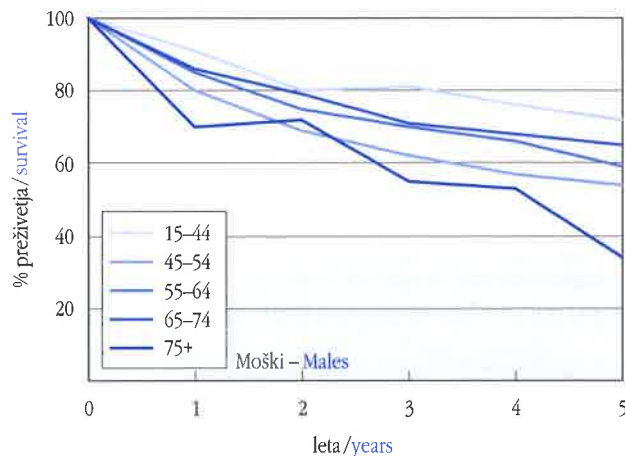
Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	80	(76-84)	59	(54-64)	51	(46-56)	89	(78-100)	75	(59-91)	74	(57-91)
1988-92	83	(79-87)	66	(61-71)	57	(52-62)	70	(55-85)	65	(49-81)	60	(43-77)
1993-97	84	(80-88)	69	(64-74)	60	(54-66)	86	(76-96)	73	(59-87)	65	(49-81)

**SLIKA 2: Relativno petletno preživetje bolnikov z rakom grla, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.****FIGURE 2: Relative five-year survival of laryngeal cancer patients diagnosed in the period 1973–1997 by stage and period of diagnosis.**

sko in v 1% kirurško, obsevalno in citostatsko. Prvo zdravljenje se je pričelo v 55% na Onkološkem inštitutu v Ljubljani, v 30% na Kliniki za otorinolaringologijo KC, v 14% v SB Maribor.

V letih 1993–97 je bilo relativno petletno preživetje za 7% večje kot v letih 1983–87 (slika 1). Preživetje se je povečalo pri omejeni in razširjeni bolezni (slika 2). Preživetje je bilo pri najstarejši skupini 2-krat manjše kot pri najmlajših. Majhno preživetje v starosti 45–54 let je najverjetneje posledica slučaja (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka grla pri moških 59,4% (57,2–61,6) in pri ženskah 56,3% (51,8–61,1), v Sloveniji pa pri moških 55,1% (46,3–65,5) in pri ženskah 78,4% (54,4–112,9). Največje preživetje pri moških je bilo 72,9% v Švici (samo v območjih registrov Basla in Ženeve) in pri ženskah 84,3% v Španiji (samo povprečje za province: Baskija, Mallorca, Navarra in Tarragona). Ob tem

**SLIKA 3: Relativno petletno preživetje bolnikov z rakom grla, zbolelih v letih 1993–1997 po starosti.****FIGURE 3: Relative five-year survival of laryngeal cancer patients diagnosed in the period 1993–1997 by age.**

ber of patients aged over 65 was higher. The stage distribution at diagnosis also changed. In the last observation period, a higher percentage of patients with regional disease was observed (Table 2).

In the period 1993–97, 96% of patients underwent specific treatment. Radiotherapy was applied as primary treatment in 53% of patients, in another 35% of patients, the primary treatment was surgery combined with radiotherapy, 10% underwent surgery alone, 2% received radio- and chemotherapy, and 1% surgery, radio- and chemotherapy. Of these patients, 55% received primary treatment at the Institute of Oncology Ljubljana, 30% at the Department of Otorhinolaryngology and Cervicofacial Surgery, UMC, Ljubljana, 21% at the Department of Maxillofacial Surgery, UMC, Ljubljana, and 14% in the General Hospital in Maribor.

The relative five-year survival was 7% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The survival increased in the patients with localized and regional disease (Figure 2).

moramo upoštevati dejstvo, da je v Sloveniji odstotek prognostično ugodnejšega raka glasilk v primerjavi z ostalim grlom manjši kot v zahodnih in severnih delih Evrope.

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Razporeditev bolnikov glede na stadij ob diagnozi se v opazovanem obdobju ni pomembno spremenila. Torej lahko izboljšanje preživetja pripišemo predvsem boljšemu zdravljenju.

Zanimivo je, da se je izid zdravljenja najbolj izboljšal pri bolnikih z omejeno boleznijo. Način kirurškega zdravljenja karcinoma grla se v opazovanem obdobju praktično ni spremenil, spremenil pa se je režim obsevanja bolnikov z zgodnjim karcinomom glasilk (1). Spremenilo se je tudi razmerje: karcinom glasilke nasproti karcinomu ostalih podlokacij grla v prid prognostično ugodnejšemu karcinomu glasilk (2).

VIRA

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In the oldest group of patients, a two-fold lower survival was observed than in younger patients. A poor survival in the age group of 45–54 years may be a sheer coincidence. (Figure 3)

According to the EUROCARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with laryngeal cancer was 59.4% (57.2–61.6) in male patients and in female patients 56.3% (51.8–61.1), while in Slovenia, it was 55.1% (46.3–65.5) in male patients and 78.4% (54.4–112.6) in female patients. The highest rates of 72.9% and of 84.3% were observed in male patients in Switzerland (only registries in Basel and Geneva) and in female patients in Spain (only in provinces: Basque Country, Mallorca, Navarra and Tarragona). At this point, it should be taken into account that the percentage of the glottic cancer in relation to the supraglottic cancer is lower in Slovenia than in Western and Northern European Countries.

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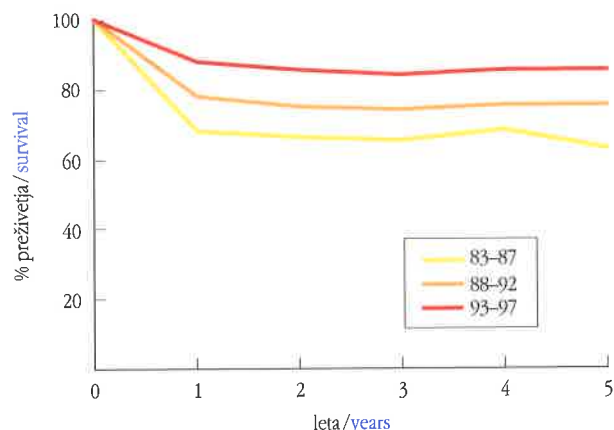
The distribution of the patients by the stage of disease at diagnosis did not change significantly in the observed period. Thus, the improved survival rates could then be well attributed to the account of better treatment results.

It is interesting that the treatment outcome improved the most in the patients with localized disease. In the observed period, no innovations of surgical treatment of the laryngeal cancer were introduced, whereas the treatment regime in radiotherapy for the patients with early glottic cancer was changed (1). Moreover, the ratio of glottic cancer vs. other laryngeal carcinomas also changed in favor of prognostically more favorable glottic carcinoma (2).

ŠČITNICA

THYROID

MKB 8 / ICD 8: 193



SLIKA 1: Relativno petletno preživetje bolnikov z rakom ščitnice, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of thyroid cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom ščitnice 215 moških in 622 žensk, od tega v letih 1993–97 78 moških in 270 žensk. V analizo ni bilo vključenih 32 (4%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka ščitnice večala. V letih 1983–87 je bila groba incidenčna stopnja 1,3/100.000 moških in 3,1/100.000 žensk, v letih 1993–97 pa 1,6/100.000 moških in 5,3/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal s 95% v letih 1983–87 na 100% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 55% papilarnih karcinomov, 14% folikularnih karcinomov, 10% anaplastičnih karcinomov, 7% karcinomov Huerthlovih celic, 6% medularnih karcinomov in 3% neopredeljenih karcinomov. Ne-Hodgkinovih limfomov je bilo 5%.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnic mlajših od 45 let. Razširjenost bolezni ob diagnozi se je spremenila. V zadnjem obdobju je bilo več bolnikov ugotovljenih z omejeno boleznijo (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 95% bolnikov. Prvo zdravljenje je bilo v 42% kombinirano: kirurško, z ¹³¹I in hormonsko, v 19% kirurško in hormonsko, v 16% samo

In the period 1983–97, a total of 215 male and 622 female patients were diagnosed with thyroid cancer; of these, 78 males and 270 females were affected with this cancer in the five-year period 1993–97. In 32 patients (4%), this cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of thyroid cancer was rising. In 1983–87, the crude incidence rate was 1.3/100,000 in males and 3.1/100,000 in females, whereas in 1993–97, it was 1.6/100,000 in males and 5.3/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the period 1993–97 was 5%, i. e. from 95% to 100%. In the years 1993–97, the percentage of papillary, follicular, anaplastic, Huerthle, medullary, non-differentiated cell carcinomas and non-Hodgkin lymphomas in microscopically confirmed thyroid cancer was 55%, 14%, 10%, 7%, 6%, 3% and 5%, respectively.

The age distribution in the group of patients included into the analysis has changed (Table 1). In the period 1993–97, the number of female patients under 45 years was higher. The stage distribution at diagnosis also changed. In the last observation period, a higher percentage of patients with localized disease was observed (Table 2).

TABELA 1: Ščitnica. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Thyroid. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87	60	0	18	10	9	14	9
	1988-92	73	1	23	8	24	11	6
	1993-97	71	1	23	13	16	16	2
Ženske Females	1983-87	149	0	40	25	31	25	28
	1988-92	191	1	62	25	40	36	27
	1993-97	261	5	83	38	51	45	39

TABELA 2: Ščitnica. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

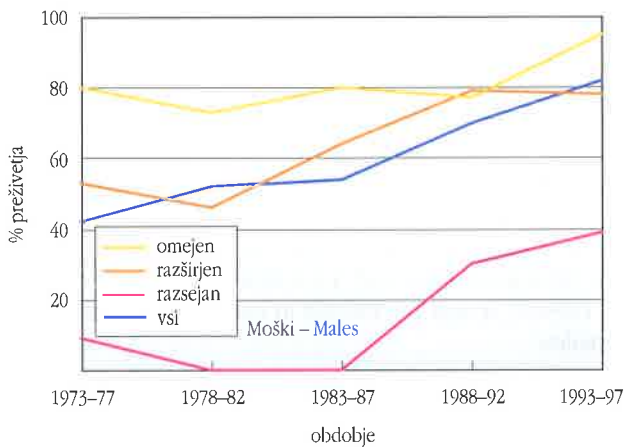
TABLE 2: Thyroid. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage					Neznan/ Unknown %			
		Omejen/ Localized %	Razširjen/ Regional %	Razsejan/ Distant %	%					
Moški Males	1983-87	60	10	16,7	35	58,3	13	21,7	2	3,3
	1988-92	73	22	30,1	36	49,3	12	16,4	3	4,1
	1993-97	71	35	49,3	27	38,0	9	12,7	0	0,0
Ženske Females	1983-87	149	56	37,6	59	39,6	26	17,4	8	5,4
	1988-92	191	82	42,9	73	38,2	32	16,8	4	2,1
	1993-97	261	146	55,9	85	32,6	28	10,7	2	0,8

TABELA 3: Ščitnica. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Thyroid. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje / Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years					Ženske / Females Leta / Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	60	(47-73)	47	(34-60)	45	(32-58)	69	(61-77)	66	(58-74)	59	(51-67)
1988-92	73	(63-83)	63	(52-74)	62	(51-73)	78	(72-84)	71	(64-78)	70	(63-77)
1993-97	85	(76-94)	76	(66-86)	73	(62-84)	86	(82-90)	80	(75-85)	77	(72-82)

Obdobje / Period	Relativno / Relative (%)											
	Moški / Males Leta / Years					Ženske / Females Leta / Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	62	(49-75)	52	(38-66)	54	(39-69)	71	(63-79)	71	(63-79)	67	(59-75)
1988-92	74	(63-85)	68	(56-80)	70	(57-83)	79	(73-85)	76	(69-83)	77	(70-84)
1993-97	86	(77-95)	81	(70-92)	82	(70-94)	88	(84-92)	85	(80-90)	86	(80-92)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom ščitnice, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.

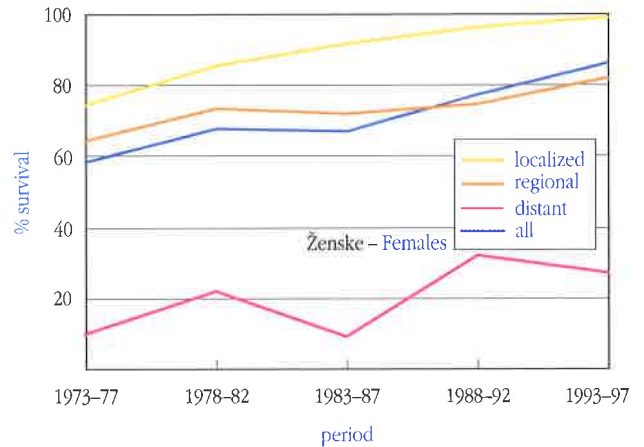


FIGURE 2: Relative five-year survival of thyroid cancer patients diagnosed in the period 1973–1997 by stage and period of diagnosis.

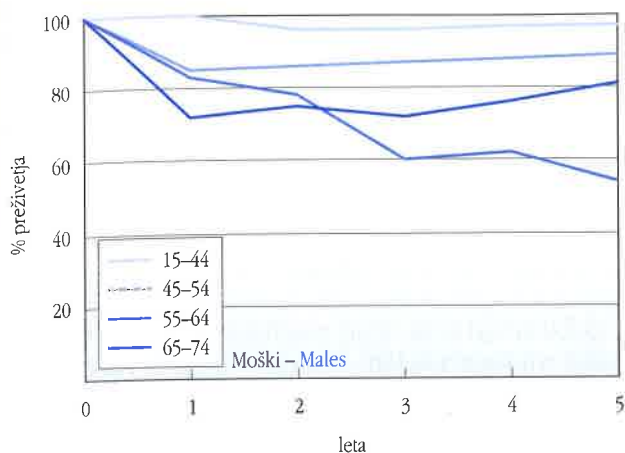
s citostatiki ali v različnih kombinacijah z ostalimi načini, v 8 % kirurško, perkutano obsevalno, z ¹³¹I in hormonsko, v 6 % samo kirurško, v 4 % samo perkutano obsevalno, v 4 % kirurško, perkutano obsevalno in hormonsko, v 1 % samo z ¹³¹I. Prvo zdravljenje se je pričelo v 73 % na Onkološkem inštitutu v Ljubljani, v 15 % na Kliničnem oddelku za torakalno kirurgijo KC, v 6 % v SB Maribor in v manjšem odstotku v SB v Slovenj Gradcu, Celju in na Kliničnem oddelku za otorinolaringologijo in cervikofacialno kirurgijo KC.

V letih 1993–97 je bilo relativno petletno preživetje za 22 % večje kot v letih 1983–87 (slika 1). Preživetje se je povečalo pri vseh stadijih bolezni (slika 2). Preživetje je bilo pri mlajših bolnikih in bolnicah pomembno večje kot pri starejših (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka ščitnice pri moških 69 % (64,4–73,8) in pri ženskah 79,3 % (77,6–81), v Sloveniji pa pri moških 80,3 % (69,9–92,1) in pri ženskah 73,7 % (67,6–80,3). Največje preživetje pri moš-

In the period 1993–97, 95% of patients underwent specific treatment; surgery, iodine- and hormone therapies were applied as primary treatment in 42% of patients, in 19% of patients, the primary treatment was surgery combined with hormone therapy, in 16% chemotherapy alone or in combination with other modalities, 8% underwent surgery, percutaneous irradiation, iodine- and hormone therapy, 6% received surgery alone, 4% percutaneous irradiation alone, 4% were treated with surgery, percutaneous irradiation, and hormone therapy, 1% received iodine treatment alone. Of these patients, 73% received primary treatment at the Institute of Oncology Ljubljana, 15% at the Department of Thoracic Surgery, UMC, Ljubljana, 6% in the General Hospital in Maribor, and a very small percentage of patients in the General Hospitals in Slovenj Gradec and Celje, and at the Departments of Otorhinolaryngology and of Cervicofacial Surgery UMC, Ljubljana.

The relative five-year survival was 22% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The sur-



SLIKA 3: Relativno petletno preživetje bolnikov z rakom ščitnice, zbolelih v letih 1993–1997 po starosti.

kih je bilo 84,9% v Islandiji in pri ženskah 89,6% v Švici (samo območji registrov Basla in Ženeve).

Marija Auersperg, Onkološki inštitut Ljubljana

Malignni tumorji ščitnice so heterogena skupina tumorjev, ki se razlikujejo tako po morfološki sliki, kot po biološki naravi. Diferencirane oblike raka (papilarni, folikularni, rak Huerthlejevih celic in medularni rak) imajo dokaj dobro napoved, posebno če jih odkrijemo, ko so še omejeni na ščitnico in jih ustrezno zdravimo (1). Za razliko od teh je anaplastični rak ščitnice izredno agresiven tumor, ki naglo preraste sosednja tkiva, zaseva v področne bezgavke in oddaljene organe ter hitro privede do smrti bolnika. Srednja preživetja teh bolnikov so manj kot 6 mesecev (2, 3, 4, 5).

Pri diferenciranih oblikah je temeljno zdravljenje operativno (6). Za »zlato standard« velja popolna odstranitev ščitnice s kapsulo vred (totalna tiroidektomija) ali »skoraj popolna« odstranitev. Pri tej operaciji ohranimo majhen delček ščitničnega tkiva pri obščitnicah, da se izognemo možnosti za okvaro njihove funkcije. Najmanjša dopustna operacija je odstranitev režnja ščitnice na strani tumorja skupaj z ovojnico in istmusom ščitnice. Ta operacija se uporablja v diagnostične namene, če narave tumorja ni mogoče pojasniti s citološko punkcijo ali pa pri prognozi zelo ugodnih tumorjih. Operativno zdravljenje je tudi najprimernejše pri zasevkih v bezgavkah. Operativno zdravljenje kombiniramo še z ^{131}J za odstranitev malih ostankov ščitničnega tkiva po operaciji in za prikaz in zdravljenje oddaljenih zasevkov. Po operaciji dobivajo bolniki doživljenjsko tiroksin za zavoro produkcije TSH, ki vzpodbuja rast ščitničnih tumorjev (1, 6). Leta 1983 smo pričeli uporabljati tudi kemoterapijo, sprva pri bolnikih z oddaljenimi zasevki, nato pa tudi pri bolnikih z razširjenimi primarnimi tumorji (7, 8). Za zanesljivo presojo vpliva kemoterapije na preživetje je ta skupina bolnikov še premajhna. Merjenje tumorskega markerja tiroglobulina (Tg) v serumu smo uvedli v pooperativno sledenje bolnikov leta 1985.

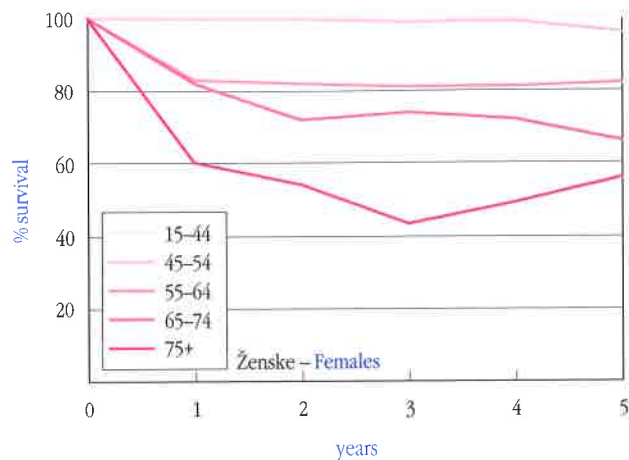


FIGURE 3: Relative five-year survival of thyroid cancer patients diagnosed in the period 1993–1997 by age.

vival increased in all disease stages (Figure 2) and was significantly higher in younger than in elderly patients (Figure 3).

According to the EURO-CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of patients with thyroid cancer was 69% (64.4–73.8) in male patients and in female patients 79.3% (77.6–81), while in Slovenia, it was 80.3% (69.9–92.1) in male patients and 73.7 (67.6–80.3) in female patients. The highest rates of 84.9% and of 89.6% were observed respectively in male patients in Iceland and in female patients in Switzerland (only registries in Basel and Geneva).

Marija Auersperg, Institute of Oncology Ljubljana

Malignant thyroid tumors are a heterogeneous group of tumors that differ in morphology and biology. Differentiated tumors (e. g. papillary, follicular, Huerthle and medullary cell carcinomas) have rather favorable prognosis, particularly when the disease is localized to the thyroid and is adequately treated (1). In contrast to the above cancer types, anaplastic thyroid cancer is extremely aggressive and rapidly invades the neighboring tissues, spreads into regional lymph nodes and distant organs and causes early death of the patient. Median survival of these patients is less than 6 months (2, 3, 4, 5).

Primary treatment for differentiated thyroid carcinoma is surgery (6). In this case, the gold standard is complete removal of the thyroid with the capsule (total thyroidectomy) or nearly total thyroidectomy. With this surgery, we generally leave some thyroid tissue nearby the parathyroids intact in order to avoid the risk of damaging their function. The minimal intervention in thyroid surgery is the excision of the thyroid lobe on the side of the tumor, together with the capsule and isthmus. This intervention is acceptable only for diagnostic purposes in cases when tumor biology cannot be defined from biopsy sample or exceptionally in tumors with favorable prognosis. Surgery is also the most adequate treatment modality for the metastatic spread in the lymph nodes. Surgery com-

Proučevali pa smo tudi predoperativne vrednosti Tg pri posameznih histoloških vrstah tumorjev in ugotovili, da je predoperativno merjenje Tg v serumu uporabno za diagnostiko folikularnih tumorjev (9).

Pri anaplastičnem raku ni znano, kakšen je najboljši način zdravljenja. Zdravljenje samo z operacijo, obsevanjem ali kemoterapijo ni uspešno (1, 2, 3, 4). Uporabljamo kombinacijo vseh treh načinov, ni pa še ugotovljeno, kakšno je njihovo najprimernejše zaporedje. Študija v Sloveniji nakazuje, da je najbolje začeti s sočasno kemoterapijo in obsevanjem in nato tumor operativno odstraniti (10). Večina anaplastičnih rakov ščitnice nastane iz predhodno diferencirane oblike, zato je zelo pomembno, da odkrivamo diferencirane oblike raka in bolnike operiramo, preden se tumor razdiferencira in postane zelo agresiven.

Na prognozo bolnikov z rakom ščitnice vplivajo številni dejavniki. Najpomembnejša sta starost bolnika in histološka vrsta tumorja. Napovedni dejavniki so še velikost tumorja, vračanje v žile in kapsulo, prisotnost metastaz, aneuploidija, način zdravljenja in spol bolnika.

V obdobju 1993–97 opažamo povečanje 5-letnega preživetja v primerjavi z 1983–87 za 22%. Na to je vplivalo več dejavnikov: zvišalo se je število žensk v starostno ugodni skupini 15–44 let (tabela 1), pri moških in ženskah je bilo več omejene bolezni, pri moških trikrat več, pri ženskah pa 1,5 krat več. Ker je bilo pri moških ugodnih dejavnikov več, se je preživetje moških lahko približalo preživetju žensk (tabela 3).

V primerih, ko je kirurg odstranil le en reženi ščitnice in je šele histološka preiskava po operaciji dokazala raka, se sedaj pogosteje odločamo za ponovno operacijo in operativno odstranitev obsežnega ostanka ščitnice in ne za odstranitev z ^{131}J , kar je bilo pogosteje v preteklih obdobjih. Prispevek k boljšemu preživetju je tudi razširjenje indikacij za zdravljenje z ^{131}J pri diferenciranem raku in sistematično pooperativno odstranjevanje malih ostankov ščitnice z ^{131}J pri vseh bolnikih razen pri mlajših od 45 let in s tumorji manjšimi od 1,5 cm.

V obdobju 1993–97 je bilo preživetje moških z razsejano boleznijo večje kot žensk, kar bi si lahko razložili s tem, da je bilo 15% žensk v starostni skupini 75 let in več, pri moških pa le 3% in da je zato v skupini žensk večji delež anaplastičnega, pri moških pa diferenciranega raka. Povečanje preživetja pri obeh spolih pa lahko pripišemo aktivnemu zdravljenju teh bolnikov s kombinacijo ^{131}J , kemoterapije, perkutanega obsevanja ter včasih tudi operacije. Prav v tej skupini je izredno pomembna timska multidisciplinarna obdelava v ustanovi, kjer so na voljo vsi načini zdravljenja, ki jih bolnik potrebuje.

Boljše preživetje pri mlajših bolnikih (slika 3) pa si lahko razložimo s stopnjo diferenciacije tumorja. Pri mlajših bolnikih je večji delež dobro diferenciranih tumorjev z boljšo prognozo.

Dejstvu, da vse bolnike z rakom ščitnice v Sloveniji ne glede na to, kje je bilo prvo kirurško zdravljenje, obravnava multidisciplinarni tim na Onkološkem inštitutu, pripisujemo nadpovprečno dobro eno- in petletno preživetje bolnikov v primerjavi s preživetjem, ki ga navaja EURO CARE v drugih devetnajstih državah. Taka obravnava bolnikov omogoča smiselno in hitro uporabo posameznih načinov zdravljenja in njihov kombinacij. Hkrati se nabirajo izkušnje članov skupine, kar

bined with postoperative iodine therapy (^{131}J), which may effectively remove small particles of the residual tumor, is applied also in the detection and treatment of distant metastases. After thyroidectomy the patients are receiving thyroxine for life in order to downregulate the production of TSH that stimulates the growth of thyroid tumors (1, 6). In 1983, chemotherapy was introduced; at first, it was applied only in the patients with distant metastases, and later on, in the patients with advanced primary tumors (7, 8). The number of patients is too small to allow an evaluation of the effect of chemotherapy on the survival. The measurement of tumor marker thyroglobulin (Tg) in the serum was introduced in postoperative follow-up as early as 1985. From the analysis of preoperative values of Tg that were also measured in individual histology tumor types, it was concluded that the measurement of Tg in the serum is useful in the diagnostics of follicular thyroid tumors (9).

So far, it has not been decided which treatment modality should be the treatment of choice for anaplastic thyroid cancer. Surgery or irradiation or chemotherapy alone have been found to be unsuccessful; therefore, a combination of all three therapies is applied although it has not been proved what sequence is the most appropriate (1, 2, 3, 4). A study performed in Slovenia showed that it is most advisable to start the treatment with concomitant radio- and chemotherapy of the tumor and then surgically remove it (10). The majority of anaplastic carcinomas of the thyroid develop from earlier differentiated cancer type. It is therefore imperative to detect thyroid cancer in its differentiated form. These patients should be immediately operated on before the tumor becomes dedifferentiated and extremely aggressive.

The prognosis of the patients with thyroid cancer may be affected by a number of factors. The most relevant ones seem to be the patient's age and histology type of the tumor. Other prognostic factors are the size of tumor, its invasion into the veins and capsule, distant metastases, aneuploidy, treatment modality and patient's sex.

In the observation period 1993–97, an increase of 22% was observed in five year-survival in comparison to that of 1983–87. This increase is the result of several factors, e.g. (i) an increased number of women in the favorable age group of 15–44 years (Table 1), (ii) at diagnosis, more cases of localized disease were detected in men (3-fold increase) as well as in women (1.5-fold increase). As more favorable factors were involved in men than in women, the survival in men could get close to that in women (Table 3).

If only one lobe is excised and postoperative histology examination confirms cancer, we usually decide to perform a second surgery and to remove the remaining thyroid rather than to apply postoperative iodine (^{131}J) treatment of the residual tumor that was earlier a frequently applied treatment modality. The improved survival may also be due to a wider range of indications for iodine (^{131}J) treatment of differentiated thyroid carcinoma and systematic postoperative removal of the remaining thyroid with ^{131}J (except in patients under 45, with tumors < 1.5 cm).

In the period 1993–97, the survival of men with metastatic disease was better than that in women. This may be explained

je za načrtovanje in uspeh zdravljenja pri tako redkih vrstah tumorjev posebej pomembno.

VIRI

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by the fact, that in the patients aged over 75 years, there were 15% of women with metastatic disease and only 3% of men, and that in women, the proportion of anaplastic cancer was higher, whereas in men, differentiated cell cancer prevailed. The improved survival in both sexes is the result of active treatment of these patients with ¹³¹I, chemotherapy, percutaneous irradiation and, occasionally, with surgery. This particular group of patients with metastatic disease requires a multidisciplinary treatment approach of a team in a health institution where all necessary treatment modalities are available to the patient.

Better survival of younger patients (Figure 3) is attributable to the degree of tumor differentiation. In younger patients, the proportion of well-differentiated tumors with favorable prognosis is higher.

All patients with thyroid carcinoma in Slovenia are referred to Multidisciplinary Advisory Team for Thyroid Carcinoma at the Institute of Oncology Ljubljana, regardless of where the primary surgery was performed. Owing to the multidisciplinary approach of this team to the patients, the one- and five-year survivals of our male patients are fairly above the average rates that are reported by EUROCARE in the remaining 19 countries. This approach to the patient allows a rational and rapid application of individual treatment modalities and of their combinations. At the same time, the members of the team are upgrading their knowledge and improving their skills, which is of utmost importance in the treatment of tumors that are so rare.

PLJUČA

LUNG

MKB 8/ICD 8: 162

V obdobju 1983–97 je zbolelo za pljučnim rakom 11.073 moških in 2209 žensk, od tega v letih 1993–97 4102 moška in 882 žensk. V analizo ni bilo vključenih 955 (7%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca pljučnega raka še večala. V letih 1983–87 je bila groba incidenčna stopnja 69,6/100.000 moških in 11,8/100.000 žensk, v letih 1993–97 pa 85,3/100.000 moških in 17,2/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal s 87% v letih 1983–87 na 93% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 39% ploščatoceličnih, 24% žlezni, 19% drobnoceličnih in 18% neopredeljenih karcinomov.

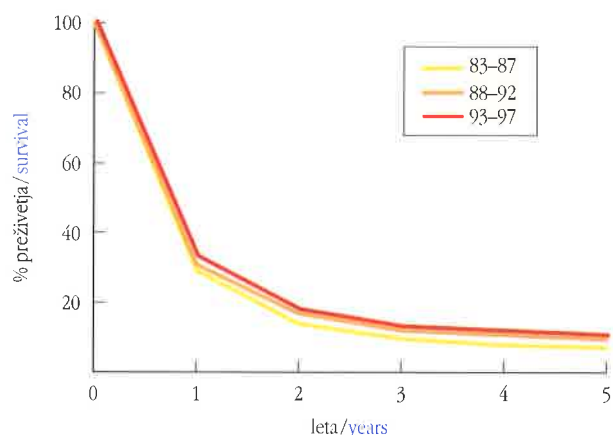
Starostna porazdelitev v analizo zajetih bolnikov se je spremenila, v zadnjih letih 1993–97 je bilo zajetih več bolnikov v starosti 65 do 74 let, ne pa starejših (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila (tabela 2). V letih 1993–97 je bilo odkrite več razsejane bolezni.

V letih 1993–97 je bilo specifično zdravljenih samo 65% bolnikov. Največ zdravljenih bolnikov je bilo med tistimi z mikrocelularnim karcinomom (79%) in najmanj med tistimi z žleznim karcinomom (66%). Prvo zdravljenje je bilo v največjem

TABELA 1: Pljuča. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Lung. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi/ Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	2959	0	116	533	1105	738	467
Males	1988-92	3481	0	139	506	1480	920	436
	1993-97	3878	1	154	586	1367	1342	428
Ženske	1983-87	513	0	34	76	145	127	131
Females	1988-92	678	0	40	86	201	214	137
	1993-97	818	1	45	106	221	298	147



SLIKA 1: Relativno petletno preživetje bolnikov s pljučnim rakom, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of lung cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 11,073 male and 2,209 female patients were diagnosed with lung cancer; of these, 4,102 males and 882 females were diagnosed with this cancer in the period 1993–97. In 955 patients (7%), lung cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of lung cancer was increasing only until 1995, when it was the highest. In 1983–87, the crude incidence rate was 69.6/100,000 in males and 11.8/100,000 in females, whereas in 1993–97, it was 85.3/100,000 in males and 17.2/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 6%, i. e. from 87% to 93%. In the years 1993–97, the percentage of squamous cell carcinomas, adenocarcinomas, microcellular and non-specified cell carcinomas in the microscopically confirmed lung cancers was 39%, 24%, 19%, and 18%, respectively.

The age distribution of patients included into the analysis has changed significantly. In the period 1993–97, the number of patients aged 65–74 years was higher (Table 1). The stage distribution at diagnosis also changed. In the last observation period, a higher percentage of patients with metastatic disease was observed (Table 2).

TABELA 2: Pljuča. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

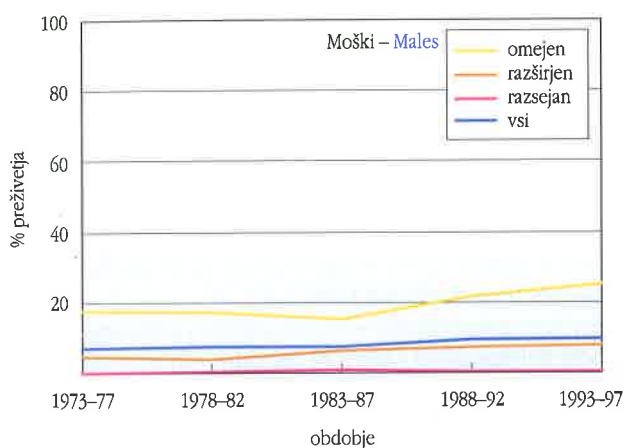
TABLE 2: Lung. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij/Stage							
			Omejen/ Localized	%	Razširjen/ Regional	%	Razsejan/ Distant	%	Neznan/ Unknown	%
Moški	1983-87	2959	848	28,7	1184	40,0	788	26,6	139	4,7
Males	1988-92	3481	997	28,6	1310	37,6	1014	29,1	160	4,6
	1993-97	3878	1026	26,5	1452	37,4	1248	32,2	152	3,9
Ženske	1983-87	513	125	24,4	169	32,9	172	33,5	47	9,2
Females	1988-92	678	156	23,0	211	31,1	269	39,7	42	6,2
	1993-97	818	212	25,9	253	30,9	308	37,7	45	5,5

TABELA 3: Pljuča. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Lung. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years					Ženske / Females Leta / Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	28	(26-30)	9	(8-10)	6	(5-7)	26	(22-30)	9	(6-12)	5	(3-7)
1988-92	30	(28-32)	11	(10-12)	8	(7-9)	30	(28-34)	12	(9-15)	9	(7-11)
1993-97	31	(29-33)	11	(10-12)	8	(7-9)	31	(28-34)	13	(11-15)	10	(8-12)

Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years					Ženske / Females Leta / Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	29	(27-31)	10	(9-11)	7	(6-8)	27	(23-31)	10	(7-13)	6	(4-8)
1988-92	32	(31-33)	12	(11-13)	9	(8-10)	30	(26-34)	14	(11-17)	11	(8-14)
1993-97	32	(31-33)	12	(11-13)	10	(9-11)	32	(28-36)	14	(11-17)	12	(9-15)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom pljuč, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

odstotku (47%) samo obsevalno, v 22% samo kirurško, 12% samo citostatsko, v 11% obsevalno in citostatsko, v 6% kirurško in citostatsko. V 59% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 22% na Kliničnem oddelku za torakalno kirurgijo KC, v 12% v Bolnišnici Golnik, v 6% v SB Maribor in v 1% na Kliničnem oddelku za nevrokirurgijo KC.

V letih 1993-97 je bilo relativno petletno preživetje za 3% večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo pri bolnikih z omejeno boleznijo. Preživetje je bilo največje pri bolnikih in bolnicah, mlajših od 45 let (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka pljuč pri moških 9,8% (9,4-10,1) in pri ženskah 9,9% (9,4-10,4), v Sloveniji pa pri moških 8,4% (7,2-9,7) in pri ženskah 9,5% (7,4-12,1). Največje preživetje pri moških je bilo 14,1% na Tirolskem v Avstriji in pri ženskah 16,4% v Švici (samo območji registrov Basla in Ženeve).

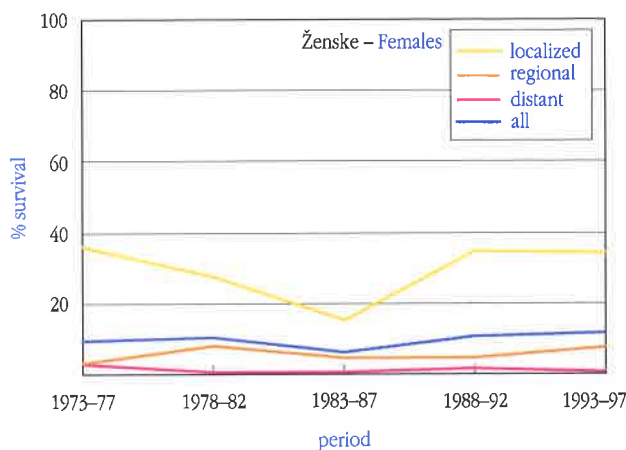
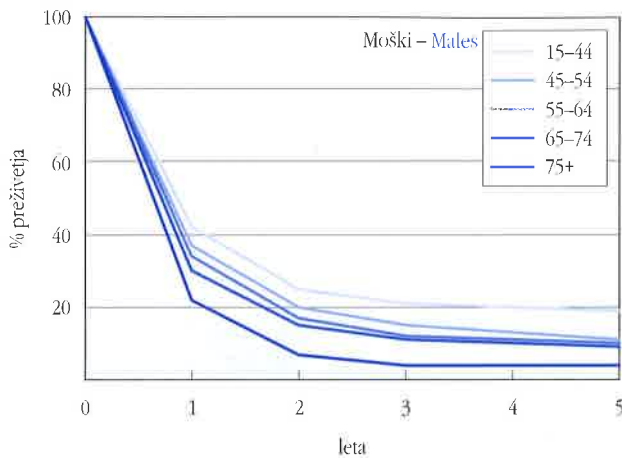


FIGURE 2: Relative five-year survival of lung cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

In the period 1993-97, 95% of patients underwent specific treatment. The highest percentage of treated patients had microcellular carcinoma (79%) and the lowest percentage (66%) adenocarcinoma. Radiotherapy alone was applied as primary treatment in the highest percentage of patients (47%), in another 22% of patients, the primary treatment was surgery alone, 12% received chemotherapy alone, 11% radio- and chemotherapy, and 6% underwent surgery and chemotherapy. Primary treatment was started at the Institute of Oncology Ljubljana in 59% of patients, in 22% at the Department of Thoracic Surgery, UMC Ljubljana, 12% in the University Clinic of Respiratory and Allergic Diseases, Golnik, 6% in the General Hospital in Maribor, and 1% at the Department of Neurosurgery, UMC Ljubljana.

The relative five-year survival rate was 3% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The survival increased in patients with localized diseases. The highest survival was observed in male and female patients under 45 years (Figure 3).



SLIKA 3: Relativno petletno preživetje bolnikov s pljučnim rakom, zbolelih v letih 1993–1997 po starosti.

Andrej Debeljak, Bolnišnica Golnik

Trend incidence pljučnega raka je posledica kadilskih razvad v preteklih desetletjih (1, 2).

Povečan odstotek mikroskopsko potrjenih pljučnih rakov si lahko razložimo z boljšimi metodami odvzemov pri perifernih tumorjih, ki se vidijo le pod rentgensko presvetlavo in jih ni videti z upogljivim bronhoskopom v bronhijih. Pri takih bolnikih se uporablja bronhoskopska igelna aspiracija perifernega tumorja in bezgavk v mediastinumu (3). V redkih primerih nam pomaga tudi bronhoalveolno izpiranje bronhija, ki vodi do perifernega tumorja (4). Kadar bronhoskopske metode odpovedo, nam pri diagnostiki pomaga transtorakalna igelna aspiracijska biopsija (5).

Pri iskanju začetnih oblik pljučnega raka nismo uspešni. Tako si lahko razložimo, da je bilo odkrite več razsejane bolezni. Da bi izboljšali odkrivanje začetnih in zgodnejših oblik pljučnega raka, smo pričeli v zadnjih letih uporabljati avtofluorescenčno bronhoskopijo ter endoskopski ultrazvok (6, 7).

Presejanje s spiralno računalniško tomografijo se v svetu uporablja študijsko za ugotavljanje zgodnjega bronhialnega karcinoma od leta 1992 (International Early Lung Cancer Action Program; I-ELCAP). Rutinskega presejanja z omenjeno metodo še ni (8).

Zamejevanje postaja bolj natančno. Pri tem nam pomaga vse bolj uporabljana računalniška tomografija ter invazivne preiskave kot sta bronhoskopska igelna aspiracija, transtorakalna igelna aspiracija mediastinuma (9) ter kirurške metode.

Ker odkrivamo razsejane oblike bolezni, je odstotek specifično zdravljenih bolnikov majhen. Premalo bolnikov z nedrobnoceličnim rakom III. in IV. stadija dobiva kemoterapijo z novejšimi in dražjimi citostatiki (10, 11).

Kirurško zdravljenje se v omenjenem obdobju ni bistveno spremenilo. Nekoliko večje relativno preživetje v zadnjem petletnem obdobju bi si lahko razlagali s kombiniranim zdravljenjem mlajših bolnikov z nedrobnoceličnim rakom pljuč, pred-

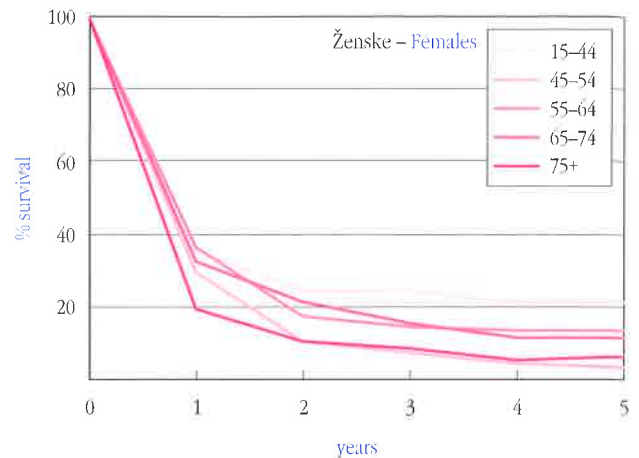


FIGURE 3: Relative five-year survival of lung cancer patients diagnosed in the period 1993–1997 by age.

According to the EUROCARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with lung cancer was 9.8% (9.4–10.1) in male patients and in female patients 9.9% (9.4–10.4), while in Slovenia, it was 8.4% (7.2–9.7) in male patients and 9.5 (7.4–12.1) in female patients. The highest rates of 14.1% and of 16.4% were observed respectively in male patients in Tyrol in Austria and in female patients in Switzerland (only registries from Basel and Geneva).

Andrej Debeljak, The University Clinic of Respiratory and Allergic Diseases, Golnik

Lung cancer incidence trend depends on smoking habits prevailing in the past decades (1, 2).

The increased percentage of microscopically confirmed lung cancer cases correlates with the introduction of the improved biopsy methods in peripheral tumors that can only be seen on X-ray but not by flexible bronchoscope. In these patients, we usually perform bronchoscopic needle aspiration biopsy of peripheral tumor and of mediastinal lymph nodes (3). In some rare cases, bronchoalveolar lavage of the bronchi, conducting to the peripheral tumor, may be helpful (4). When bronchoscopy fails in diagnostics, we can use transthoracic needle aspiration biopsy (5).

The detection of early stages of lung cancer has not been successful so far. This may explain the reason why lung cancer is more often detected in advanced stages. In order to improve the detection of the disease in its initial and early stages, we have introduced autofluorescence bronchoscopy and endoscopic ultrasound examination (6, 7).

In the detection of early bronchial carcinoma, screening by spiral computer tomography has been used since 1992 (International Early Lung Cancer Action Program; I-ELCAP), but for research purpose only. This method has not been applied as a routine in screening (8).

vsem III A stadija, ki so bili operirani, poleg tega pa so dobivali tudi citostatsko zdravljenje.

Za izboljšanje preživetja bolnikov s pljučnim rakom moramo svoje napore usmeriti v iskanje začetnih in zgodnjih oblik bolezni. Uporabiti moramo čim natančnejše zamejevanje ter kombinirane načine zdravljenja tudi z uporabo novejših citostatikov ter uspešnejših načinov obsevalnega zdravljenja.

Janez Eržen, Klinični oddelek za torakalno kirurgijo KC

V opazovanem 15-letnem obdobju se je incidenca pljučnega raka večala. Vzporedno z večanjem števila bolnikov se je povečevalo tudi število pljučnih resekcij. Leta 1985 smo na Kliničnem oddelku za torakalno kirurgijo v Ljubljani naredili 105 pljučnih operacij zaradi raka, leta 1999 pa 233. Napovedujejo pa, da se bo zbolevanje za pljučnim rakom pri moških do leta 2009 pričelo zmanjševati (1), medtem ko bo pri ženskah naraščalo (2). Napoved za moške pa zbuja dvome zaradi nepredvidljivosti števila kadilcev, ki bodo in so v omenjenem obdobju kajenje opustili, in števila novih kadilcev. Pri slednjih je zelo pomembna tudi starost začetka kajenja. Znano je, da so kadilci, ki začnejo kaditi mlajši od 15 let, dvakrat bolj ogroženi s pljučnim rakom kot tisti, ki so pričeli s kajenjem po 20. letu starosti (12).

K povečanju števila bolnikov starih 65–74 let v letih 1993–97 je poleg preteklih kadilskih navad prispevalo tudi izboljšanje tehničnih in diagnostičnih zmogljivosti, ki omogočajo varne in točne preiskave tudi pri težjih bolnikih.

Novi diagnostični postopki (endobronhijalni ultrazvok, transtorakalno in peribronhijalna biopsija s tanko iglo) in izboljšava ter povečano število računalniških tomografov (spiralni CT) pa zagotavljajo bolj natančno določitev bolezenskega stadija in s tem porast števila novo odkritih bolnikov z razsejano boleznijo. Ko bomo tudi pri nas uvedli pozitronsko emisijsko tomografijo, se bo to število še povečalo in pripomoglo k boljšim odločitvam glede zdravljenja. Predvsem se bo zmanjšalo število nepotrebnih operacij.

Odstotek primarno operiranih bolnikov (22%) je podoben kot drugje v Evropi. Na splošno velja, da je vsak peti bolnik s pljučnim rakom kandidat za operacijo (13).

Izboljšanje petletnega preživetja v obdobju 1993–97 je posledica večje točnosti določanja bolezenskega stadija, boljše izbire bolnikov za operacijo in manjše zgodnje pooperacijske smrtnosti. K temu pa je doprineslo tudi neoadjuvantno in adjuvantno zdravljenje s citostatiki, ki se čedalje pogosteje uporablja tudi pri nas.

Matjaž Zwitter, Onkološki inštitut Ljubljana

Kako gleda na objektivne podatke o incidenci, razširjenosti bolezni in rezultatih zdravljenja zdravnik, ki mu zdravljenje pljučnega raka predstavlja večino strokovnega dela? Predvsem bi si želel, da bi ti podatki pri bralcu ne spodbudili terapevtskega nihilizma, pač pa trezno, objektivno presojo o tem, kje smo in kateri naj bodo cilji naše diagnostike in zdravljenja. O pomenu, potencialni koristi in težavni izvedbi preprečeva-

At present, staging of the disease has improved considerably. This is mainly due to more frequent use of computer tomography (CT) and invasive methods of examination, such as bronchoscopic needle aspiration biopsy, transthoracic needle aspiration biopsy of the mediastinum (9) and surgery.

As the disease is generally detected in its disseminated stage, the percentage of patients receiving specific treatment is relatively low. Among the patients with stage III. and IV. non-small cell lung cancer, too few are receiving chemotherapy with the new and more costly cytostatics (10, 11).

In the last observation period, surgical treatment did not significantly change. The reasons for a partial improvement of relative survival in the last five-year observation period may lie in the combined treatment of relatively younger patients with non-small cell lung cancer, mostly of stage IIIA, who underwent surgery and were receiving cytostatics.

The survival of patients with lung cancer may well be improved by detecting the disease in its initial and early stages, by disease staging as accurate as possible, and by applying combined treatment modalities, including chemotherapy with the new cytostatics and more effective treatment regimes in radiotherapy.

Janez Eržen, Department of Thoracic Surgery, UMC Ljubljana

In the observed 15-year period, the lung cancer incidence was constantly rising. With the increased number of lung cancer patients, the amount of lung resections increased, too. In 1985, a total of 105 lung resections for cancer were performed, whereas in 1999, the number of these operations rose to 233 resections. It is predicted that, by 2009, the lung cancer incidence will start to decrease in males (1) and to increase in females (2). Such prognosis for males may nevertheless be unreliable because of unpredictable number of smokers who will give up or already have given up smoking in the period referred to and of the number of new smokers. In the latter, the age at which they start to smoke is essentially important. It is generally recognized that those who start to smoke before the age of 15 years are exposed to a two-fold risk for lung cancer in comparison to those who start to smoke after the age of 20 (12).

In the period 1993–97, the increased number of lung cancer patients in the age-group of 65–74 years is, in addition to the smoking habits in the past, also due to the improvement in technology and diagnostics potentials that allow safe and accurate examinations even of seriously-ill patients.

New diagnostic procedures (bronchoscopic ultrasonography, transthoracic and peribronchial fine needle biopsy), upgrading of computer tomography (spiral CT) and more CT machines available allow a more accurate disease staging, thereby creating also an increase in the newly detected cancer patients with the disseminated disease. With the introduction of positron emission tomography (PET) in Slovenia, the number of newly detected cancer cases will grow further which will facilitate the decision-making in treatment. The first

nja kajenja je bilo napisano že veliko, zato naj se v tem komentarju omejimo na možnosti uspešnejšega zdravljenja.

Če naj ostanemo na realnih tleh, potem moramo za začetek jasno povedati, da bo med vsemi raki pljučni rak tudi v prihodnjih desetletjih po številu umrlih še vedno na prvem mestu. Pri večini bolnikov bo tudi v bodoče cilj zdravljenja le olajšanje težav in ureditev podpornega in simptomatskega zdravljenja. Boljšega, primernejšega zdravljenja teh bolnikov ne moremo videti v krivuljah petletnega preživetja. Spremembe pa lahko pričakujemo pri manjšini bolnikov, za katero se zdi, da je bolezen sorazmerno omejena. Pri teh bolnikih je najprej na mestu mnogo natančnejša diagnostika, kot jo izvajamo danes. Razširjenost bolezni bomo ugotovljali z novimi endoskopskimi tehnikami, z računalniško tomografijo visoke ločljivosti, z dosledno uporabo scintigrafije okostja in računalniške tomografije centralnega živčevja in s pozitronsko emisijsko tomografijo. Natančnejša diagnostika nam bo omogočila, da bomo nove učinkovite, vendar zahtevne, drage in tudi za bolnika obremenjujoče načine zdravljenja kar najbolj racionalno usmerjali. Prav ob domnevno omejeni bolezni bo bolniku v največjo korist skrbno pripravljen načrt kombinacije uvodnega citostatskega zdravljenja, kirurgije in obsevanja.

Krivulje preživetja nas utrjujejo v prepričanju, da skoraj ni bolnika s pljučnim rakom, za katerega bi lahko mirno trdili, da ima dobro prognozo. Povedo nam, kako nesmiselno je razlikovanje na »kirurške« in »onkološke« bolnike. Kažejo nam, kako nujno je tudi pri pljučnem raku tesnejše sodelovanje med zdravniki, ki se ukvarjajo s preventivo, z diagnostiko in z različnimi načini zdravljenja.

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benefit of PET technology will be a much smaller number of unnecessary surgical interventions.

The percentage of primary surgical treatment in Slovenia is similar to the percentages in the rest of Europe. In general, one of five patients with lung cancer is the candidate for surgical treatment (13).

A better survival in the period 1993-97 may be attributed to the improved accuracy of disease staging, effective selection of proper candidates for surgical treatment, and low postoperative mortality. Among significant contributors to the improved five-year survival are also adjuvant and neo-adjuvant treatment with cytostatics. Both have started to be used more and more frequently in Slovenia.

Matjaž Zwitter, Institute of Oncology Ljubljana

What attitude does a physician who is mainly engaged with lung cancer treatment take towards factual data on cancer incidence, cancer staging and cancer treatment outcome? I wish that these facts would not promote a therapeutic nihilism, but would rather let the reader to make a sound and sensible judgment on the current state of the art in cancer diagnostics and treatment and on the aims that should be met. Significance of antismoking campaigns, their potential benefits and difficulties in launching them have been already largely discussed; in this analysis, we shall therefore focus on the prospects of successful treatment.

Were we to remain on firm footing, we would, at the very outset, say it clearly that, in the coming decades, lung cancer will still rank first by mortality rate among all cancers. The majority of patients will be mainly receiving palliative, supportive and symptomatic treatments. Looking at the curves showing the five-year survival of these patients, we can hardly think of any better or more adequate treatment for them. Hopefully, the changes may be expected in a smaller group of patients with seemingly localized disease. In these patients, the diagnostics should be carried out more accurately and carefully than in everyday practice. In these cases, the disease staging will be performed using the latest endoscopic techniques, computer tomography of high resolution, regular whole-skeleton scintigraphy as well as positron emission tomography and computer tomography of the central nervous system. With more precise diagnostics we will be able to apply most sensibly the latest, highly effective, demanding, and costly treatment modalities though they are patient-unfriendly. The greatest benefit for the patient who is believed to have local disease is undoubtedly a carefully designed treatment plan combining initial chemotherapy with surgery and postoperative radiotherapy.

The survival curves make us believe that there is hardly any lung cancer patient who could be claimed to have a favorable prognosis. But, they do inform us how useless it is to classify the lung cancer patients as *surgical* and *oncological*. And they also highlight the urgent need for a close cooperation among the physicians involved in lung cancer prevention, diagnostics and different treatment modalities

DOJKA

BREAST

MKB 8/ICD 8: 174

V obdobju 1983–97 je zbolelo za rakom dojk 96 moških in 10,324 žensk, od tega v letih 1993–97 46 moških in 4041 žensk. V analizo ni bilo vključenih 263 (2,5%) bolnic, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka dojk večala. V letih 1983–87 je bila groba incidenčna stopnja 0,4/100.000 moških in 57,9/100.000 žensk, v letih 1993–1997 pa 1/100.000 moških in 79/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov je bil v letih 1983–87 97%, v letih 1993–97 pa 96%. Med mikroskopsko potrjenimi je bilo v letih 1993–97 99% karcinomov, 9 primerov ne-Hodgkinovih limfomov in 4 primeri filoidnih cistosarkomov.

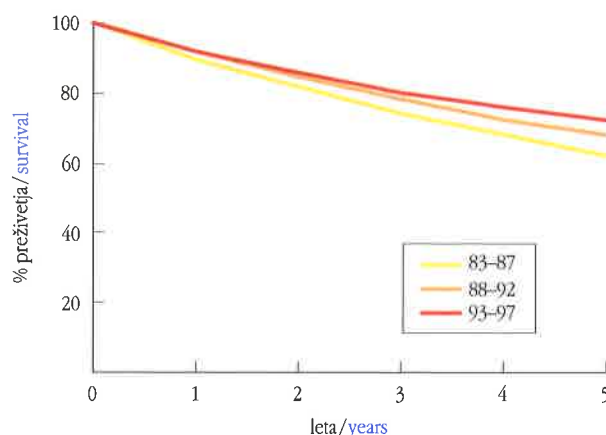
Starostna porazdelitev v analizo zajetih bolnic se je spremenila, v letih 1993–97 je bilo zajetih več starejših bolnic (tabela 1). Razširjenost bolezni ob diagnozi se je le malo spremenila. V zadnjem obdobju je bilo v omejenem stadiju bolezni odkritih samo za 3% več primerov bolezni kot v prvem (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 97% bolnic. Prvo zdravljenje je bilo v 17% kirurško in citostatsko, v 16% samo kirurško, v 15% kirurško in hormonsko, v 10% kirurško, obsevalno in citostatsko, v 9% kirurško in obsevalno, v 9% samo hormonsko, v 6% kirurško, obsevalno in hormonsko, v 6% kirurško, citostatsko in hormonsko, v 4% kirurško, obsevalno,

TABELA 1: Dojka. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Breast. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi/ Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški Males	1983-87	21	0	0	2	8	4	7
	1988-92	29	0	3	2	10	6	8
	1993-97	45	0	4	7	13	18	3
Ženske Females	1983-87	2762	0	432	660	777	505	388
	1988-92	3342	0	531	716	861	712	522
	1993-97	3958	0	565	843	945	1011	594



SLIKA 1: Relativno petletno preživetje bolnikov z rakom dojk, zbolelih v letih 1973–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of breast cancer patients diagnosed in the period 1973–1997 by period of diagnosis.

In the period 1983–97, a total of 96 male and 10,324 female patients were diagnosed with breast cancer; of these, 46 males and 4,041 females were diagnosed in the period 1993–97. In 263 patients (2.5%), breast cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of this cancer was increasing. In 1983–87, the crude incidence rate was 0.4/100,000 in males and 57.9/100,000 in females, whereas in 1993–97, it was 1/100,000 in males and 79/100,000 in females.

The percentage of the microscopically confirmed cases in 1983–87 was 97%, whereas in the observation period 1993–97, it was 96%. In the years 1993–97, the percentage of carcinomas in the microscopically confirmed cases was 99%; 9 cases were non-Hodgkin lymphomas and 4 were phylloid cytosarcomas.

The age distribution of patients included into the analysis has changed. In the period 1993–97, the number of elderly patients included in the analysis was higher (Table 1). The stage distribution at diagnosis slightly changed. In the last observation period only a 3% higher percentage of patients with localized disease was observed in comparison to the first observation period (Table 2).

TABELA 2: Dojka. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

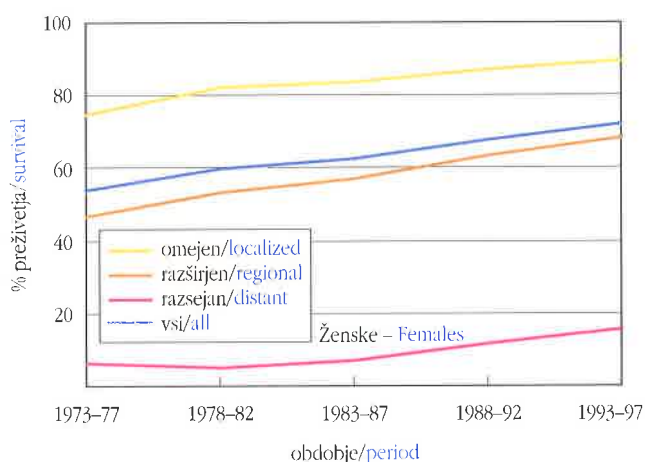
TABLE 2: Breast. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij / Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%			
Moški Males	1983-87	21	6	28,6	10	47,6	4	19,0	1	4,8
	1988-92	29	11	37,9	13	44,8	5	17,2	0	0,0
	1993-97	45	14	31,1	25	55,6	5	11,1	1	2,2
Ženske Females	1983-87	2762	1116	40,4	1310	47,4	295	10,7	41	1,5
	1988-92	3342	1410	42,2	1539	46,1	339	10,1	54	1,6
	1993-97	3958	1721	43,5	1798	45,4	397	10,0	42	1,1

TABELA 3: Dojka. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Breast. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	67	(46-88)	43	(21-65)	33	(12-54)	88	(87-89)	70	(68-72)	56	(54-58)
1988-92	86	(73-99)	72	(55-89)	55	(36-74)	90	(89-91)	73	(71-75)	60	(58-62)
1993-97	89	(80-98)	56	(41-71)	48	(33-63)	90	(89-91)	75	(74-76)	64	(62-66)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	72	(50-94)	53	(26-80)	47	(18-76)	90	(89-91)	75	(74-76)	62	(61-63)
1988-92	90	(80-100)	84	(68-100)	71	(47-95)	92	(91-93)	78	(77-79)	68	(67-69)
1993-97	92	(80-100)	62	(46-78)	58	(40-76)	92	(91-93)	81	(79-83)	72	(70-74)



SLIKA 2: Relativno petletno preživetje bolnic z rakom dojk, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

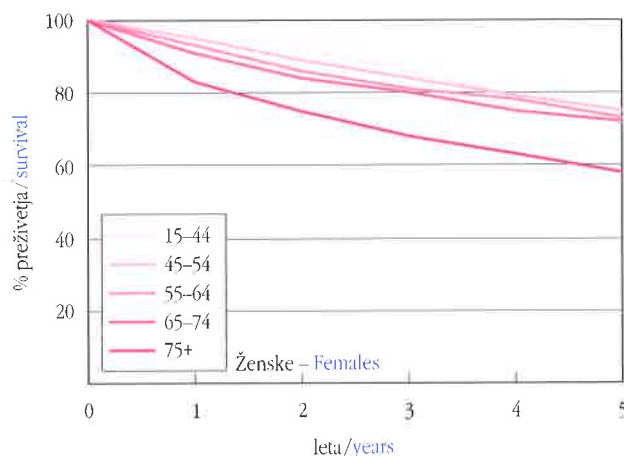
FIGURE 2: Relative five-year survival of breast cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

citostatsko in hormonsko, v 2% samo citostatsko, v 2% obsevalno, citostatsko in hormonsko, v 2% citostatsko in obsevalno in v 1% citostatsko in hormonsko.

V 61% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 17% v SB Maribor, po 7% v SB v Šempetru pri Novi Gorici in v Celju, v 4% v SB v Novem mestu, v 2% v SB v Slovenj Gradcu in v dobrem odstotku v Bolnišnici za ženske bolezni in porodništvo v Postojni. Posamezne bolnice so pričele s prvim zdravljenjem še na Kliničnem oddelku za nevrokirurgijo KC, Kliničnem oddelku za abdominalno kirurgijo KC in v drugih splošnih bolnišnicah Slovenije (1%).

V letih 1993-97 je bilo relativno petletno preživetje za 10% večje kot v letih 1983-87, razlike v 1-3 letnem preživetju pa so bile manjše (slika 1). Preživetje se je povečalo pri vseh stadijih bolezni (slika 2). Preživetje je bilo pri starih 75 let in več za 15% manjše kot pri mlajših (slika 3).

Izsledki študije EUROCARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje



SLIKA 3: Relativno petletno preživetje bolnic z rakom dojk, zbolelih v letih 1993-1997 po starosti.

FIGURE 3: Relative five-year survival of breast cancer patients diagnosed in the period 1993-1997 by age. Females

In the period 1993-97, 97% of patients underwent specific treatment. Surgery and chemotherapy were applied as primary treatment in 17%, in 16% of patients surgery only, in 15% of patients the primary treatment was surgery and hormonal therapy, 10% received surgery, radio- and chemotherapy, 9% underwent surgery and radiotherapy, 9% received hormonal therapy alone, 6% underwent surgery, radio- and hormonal therapy, 6% underwent surgery, chemotherapy and hormonal therapy, 4% received surgery, radio-, chemo- and hormonal therapy, 2% chemotherapy only, 2% radio- and chemotherapy, 2% radio-, chemotherapy and hormonal therapy, and 1% chemo- and hormonal therapy.

Primary treatment was started at the Institute of Oncology Ljubljana in 61% of patients, in 17% in the General Hospital in Maribor, in 7% in the General Hospitals Šempeter pri Novi Gorici and in Celje, in 4% in the General Hospital of Novo mesto, in 2% in the General Hospital of Slovenj Gradec and in 1% in the Hospital of Postojna. A few patients (all together

za raka dojke pri moških 74,4% (68,5–80,9) in pri ženskah 74,8% (74,3–75,3), v Sloveniji pa pri moških 57,4% (37,5–88) in pri ženskah 65,6% (63,1–68,3). Največje preživetje pri moških je bilo 86,4% v Španiji (samo na območju provinc: Baskija, Mallorca, Navarra in Tarragona), pri ženskah pa 81,6% na Švedskem.

Tanja Čufer, Onkološki inštitut Ljubljana

Pri ženskah in pri moških se razmerje med deležem omejene in razširjene bolezni v 15-letnem opazovanem obdobju skorajda ni spremenilo. Še vedno je pri več kot polovici slovenskih žensk (tabela 2) bolezen odkrita šele v razširjenem ali razsejanem stadiju bolezni. Zaskrbljujoče je, da v opazovanem obdobju ni bilo večjih premikov k zgodnejšemu odkrivanju bolezni, ker se je prav v letih 1993–97 povečalo število mamografskih centrov v državi.

Glede na nespremenjeno stanje na področju zgodnje diagnostike raka dojke so razlike v preživetju ogledalo zdravljenja. 10-odstotno izboljšanje 5-letnega relativnega preživetja vseh bolnic, zdravljenih v obdobju 1993–97, v primerjavi z bolnicami, zdravljenimi v letih 1983–87, pomeni za okoli četrtno zmanjšano umrljivost zaradi raka dojke. Meta-analiza, objavljena leta 1992, je jasno pokazala, da dopolnilno sistemsko zdravljenje za okoli tretjino zmanjša umrljivost zaradi raka dojke, absolutna dobrobit pa je odvisna od stadija bolezni (1, 2). Slika 5-letnih preživetij po stadiju glede na obdobje diagnoze pokaže, da so bile dobrobiti dopolnilnega sistema zdravljenja naše bolnice deležne že v letih 1988–92, še pred objavo te meta-analize. To je posledica dejstva, da so bile takrat številne bolnice vključene v klinične raziskave dopolnilnega sistema zdravljenja in so bile deležne koristi tega zdravljenja še preden je bilo uvedeno v rutinsko prakso. Nadaljnje izboljšanje preživetja v letih 1993–97 je posledica uvedbe antraciklinov, ki, kot je dokazano v meta-analizi, objavljeni leta 1998, še za 12% zmanjšajo umrljivost za rakom dojke (3).

Pregled po stadijih pa pove, da smo dobrobiti dopolnilnega zdravljenja povsem zadovoljivo izkoristili pri bolnicah z razširjeno boleznijo, premalo pa pri bolnicah z omejeno boleznijo. Verjetno je predolgo veljala dogma, da imajo vse bolnice z negativnimi pazdušnimi bezgavkami dobro prognozo in jih ni smiselno izpostavljati neželenim učinkom kemoterapije in hormonske terapije. To potrjuje tudi število s kemoterapijo in hormonsko terapijo zdravljenih bolnic. V obdobju 1993–97, ko je bilo povsem jasno (1, 2), da imajo vse bolnice z operabilnim rakom dojke korist od dopolnilnega zdravljenja, je v okviru prvega zdravljenja prejelo kemoterapijo samo 44% bolnic.

Ohrabrujoče je povečanje 5-letnega preživetja bolnic z razsejano boleznijo v zadnjem opazovanem obdobju. Te bolnice sicer niso ozdravljene, podatki pa potrjujejo, da imajo z uvedbo učinkovitejšega sistema zdravljenja (antraciklini, taksani) sedaj veliko večje možnosti dolgotrajnejših zdravitev (4). Večje izboljšanje preživetja pri razsejani kot pri omejeni bolezni je verjetno posledica dejstva, da novih učinkovitih zdravil nismo v zadostni meri uporabili pri bolnicah z omejeno boleznijo.

Preživetje bolnic, starejših od 75 let, je za 15% manjše kot pri mlajših. To kaže, da te bolnice niso deležne primerne preve-

er 1%) started primary treatment at the Departments of Neurosurgery and of Abdominal Surgery, UMC in Ljubljana and in other general hospitals of Slovenia.

The relative five-year survival rate was 10% higher in the years 1993–97 than in the years 1983–87. The differences in 1–3-year survivals were lower (Figure 1). The survival increased in patients with the diseases at all stages (Figure 2). The survival in the patients over 75 years was 15% lower than that in younger patients (Figure 3).

According to the EURO-CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with breast cancer was 74.4% (68.5–80.9) in male patients and in female patients 74.8% (74.3–75.3), while in Slovenia, it was 57.4% (37.5–88) in male patients and 65.6 (63.1–68.3) in female patients. The highest rates of 86.4% and of 81.6% were observed respectively in male patients in Spain (only regions: Basque Country, Granada, Mallorca, Murcia, Navarra and Tarragona) and in female patients in Sweden.

Tanja Čufer, Institute of Oncology Ljubljana

Both in female and male patients, the ratio between localized and regional disease has not significantly changed in the 15-year observation period. In more than half of female patients in Slovenia, breast cancer is detected in its regional or advanced stage (Table 2). Moreover, what is worrying is the fact that, in the last observation period, no significant progress was observed in early detection of the disease, though the number of mammographic health centers in the country increased just in the years 1993–97.

Considering the unchanged situation in the early detection of breast cancer, the differences in survival are a true reflection of treatment impact. In comparison to the survival of patients treated for breast cancer in the period 1983–87, a 10% improvement of relative five-year survival of the patients treated in the years 1993–97 is, in fact, the mortality rate reduced by almost 25%. Meta-analysis published in 1992 clearly demonstrated that the adjuvant systemic treatment reduces breast cancer mortality rate by about one third, whereas the absolute benefit remains dependent upon the stage of the disease (1, 2). A closer look at five-year survival by stage of the disease indicates that the patients in Slovenia benefited from adjuvant systemic treatment already in the years 1988–92, i. e. long before the publication of the above meta-analysis. This may be due to the fact that, at that time, a lot of patients were included in clinical studies on adjuvant systemic treatment; hence, they had benefited from that treatment modality before it was introduced as a routine in everyday practice. Further improvements of survivals in the years 1993–97 are attributable to the application of anthracyclines; this drug, as it was proved in the meta-analysis published in 1998, reduces additionally the breast cancer mortality rate by 12% (3). The analysis by stage confirms that we have satisfactorily exploited the benefits of adjuvant systemic treatment in the patients with regional disease, but less sufficiently in the patients with localized disease. It seems that the guidelines advocating that the patients with negative axillary lymph nodes have favorable prognosis and therefore should not be unnecessarily exposed to side-effects of

ga zdravljenja. Razlog lahko iščemo v premajhni uporabi hormonske terapije in v predsodku, da kemoterapija ni primerno zdravljenje za stare bolnice. Na problem nezadostnega zdravljenja in slabega preživetja starih bolnic so opozorili tudi drugje po svetu (5). Izoblikovali so že posebne primernejše smernice zdravljenja starih bolnic. Preživetje bolnic v Sloveniji je odvisno od tega, koliko bomo te smernice sprejeli in jim sledili.

Preživetje bolnic z rakom dojk je mogoče izboljšati z zgodnejšim odkrivanjem bolezni in s sprotnim uvajanjem novih načinov sistemskega zdravljenja. V Sloveniji lahko še izboljšamo zgodnje odkrivanje raka dojk. Novi načini sistemskega zdravljenja so se uvajali sproti. Optimalnega tretjinskega zmanjšanja umrljivosti pa nismo dosegli pri bolnicah z omejeno boleznijo in pri starih bolnicah. Te bolnice verjetno niso bile v zadostni meri deležne dopolnilnega zdravljenja.

Jurij Lindtner, Onkološki inštitut Ljubljana

Povečano 5-letno preživetje pripisujem predvsem modernim, agresivnejšim načinom zdravljenja in manj le za 3% večjemu številu bolnic v omejenem stadiju bolezni. Preživetje pri starih bolnicah, pri katerih je opisano zdravljenje težje izvedljivo, potrjuje to sodbo.

Ugotovitev, da spada Slovenija na podlagi izsledkov raziskave EURO-CARE-3 še vedno med dežele s podpovprečnim relativnim starostno standardiziranim preživetjem, je ob premajhnem odstotku bolnic, odkritih z omejeno boleznijo, morda moč razložiti tudi z dejstvom, da načini ravnanja z bolnicami, ki se po prejšnjem odstavku kažejo kot učinkovitejši, ne dosežejo vseh bolnic.

Elga Majdič, Onkološki inštitut Ljubljana

V obdobju 1983–97 je prišlo tudi do sprememb v načinu lokalnega zdravljenja operabilnega raka dojk. Zelo se je zmanjšalo število radikalnih mastektomij in povečalo število delnih resekcij dojk s pooperativnim obsevanjem. Na ta način smo dosegli boljšo kakovost življenja, po meta-analizi radioterapevtskih študij leta 2000 (6, 7) pa pooperativno obsevanje pozitivno vpliva tudi na preživetje. Tako kot sistemskega je bila tudi obsevalnega zdravljenja v manjši meri deležna starejša populacija.

chemotherapy and hormonal therapy was far too long in practice. The same issue was supported also by total number of patients who were treated with chemotherapy and hormonal therapy; in the period 1993–97, when it was already evident (1, 2) that all patients with operable breast cancer may benefit from adjuvant treatment, only 44% of breast cancer patients received chemotherapy as primary treatment.

The improvement of five-year survival of the patients with metastatic disease in the latest observation period is encouraging. These patients are not considered as cured; hence, from these data, it may be concluded that their prospects for long-term remission are much greater (4) with the application of more effective systemic treatment (anthracyclines, taxanes). Greater improvement in survival of the patients with metastatic disease than of those with localized disease may be due to the fact that, in the treatment of patients with localized disease, we did not apply the latest most effective drugs as much as we should.

The survival of patients over 75 years is lower by 15% in comparison to younger patients. This may be the indication that these patients had not received a proper primary treatment. Moreover, the reasons for their lower survival may lie simply in the restrictions of application of hormonal therapy and in the prejudice that chemotherapy is not an appropriate treatment modality for elderly patients. This problem of inadequate treatment and poor survival of elderly breast cancer patients has been observed also elsewhere in the world (5). Therefore, special guidelines, more appropriate for the treatment of elderly patients, have already been designed. The survival of these patients in Slovenia depends on to what extent we shall adopt and follow these guidelines.

The survival of breast cancer patients may be improved by earlier detection of the disease and concurrent introduction of updated regimes of systemic treatment. In Slovenia, early detection of breast cancer can be further improved. As to the new regimes of systemic treatment, we were introducing them into practice as they were appearing. The optimal, one-third decrease in mortality rate of the patients with localized disease and of elderly patients was not achieved. Apparently, these patients did not receive adequate adjuvant treatment.

Jurij Lindtner, Institute of Oncology Ljubljana

In my view, the increase of five-year survival is attributable to up-to-date, aggressive treatment modalities and to a lesser extent to only 3% increase of patients with localized disease. The survival rates of elderly patients who can hardly be treated with these modalities supports this view.

The observation that, according to the EURO-CARE-3 study results for the period 1990–94, Slovenia ranks among the countries and regions with the age-standardized relative survival rate that is below the average rate, can be explained by the fact that not all of the breast cancer patients with the disease detected in localized stage, despite low percentage of them, were eligible for the treatment modalities that are described in the above paragraph as more effective.

VIRI

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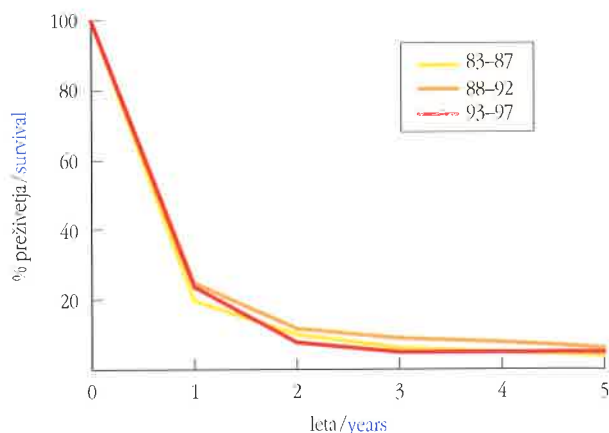
Elga Majdič, Institute of Oncology Ljubljana

In the years 1983-97, several changes were introduced into the local treatment of operable breast cancer. The number of radical mastectomies dropped considerably, whereas the number of partial resections followed by postoperative radiotherapy increased. That way, the quality of life of patients improved significantly; moreover, according to the meta-analysis of radiotherapy studies from the year 2000 (6, 7), postoperative radiotherapy has a favorable effect on the survival. Elderly patients, though to a smaller extent, were also receiving systemic treatment as well as postoperative radiotherapy.

POŽIRALNIK

ESOPHAGUS

MKB 8 / ICD 8: 150



SLIKA 1: Relativno petletno preživetje bolnikov z rakom požiralnika, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of esophageal cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom požiralnika 1186 moških in 210 žensk, od tega v letih 1993–97 387 moških in 66 žensk. V analizo ni bilo vključenih 165 (8,5%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju je bila incidenca raka požiralnika ustaljena. V letih 1983–87 je bila groba incidenčna stopnja 8,6/100.000 moških in 1,3/100.000 žensk, v letih 1993–97 pa 8/100.000 moških in 1,3/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal s 83% v letih 1983–87 na 89% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 81% ploščatočeličnih, 8% žleznih in 8% neopredeljenih karcinomov.

V zadnjem obdobju 1993–97 je bilo v analizo zajetih več starejših bolnikov (tabela 1) in več z že razširjeno boleznijo ob diagnozi (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih le 60% bolnikov. Prvo zdravljenje je bilo največkrat samo obsevalno (38%) ali samo kirurško (36%) ali kombinacija obojega. Operirani so bili na Kliničnem oddelku za torakalno kirurgijo KC ter v splošnih bolnišnicah Maribor in Celje, obsevani pa na Onkološkem inštitutu v Ljubljani.

V letih 1993–97 je bilo relativno petletno preživetje enako kot v letih 1983–87, le enoletno se je povečalo za 5% (slika 1).

TABELA 1: Požiralnik. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Esophagus. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87 1988-92 1993-97	364 369 360	0 0 0	17 17 11	96 66 60	111 144 160	79 79 102	61 63 27
Ženske Females	1983-87 1988-92 1993-97	54 64 56	0 0 0	0 1 2	2 10 3	16 15 9	18 15 19	18 23 23

In the period 1983–97, a total of 1,186 male and 210 female patients were diagnosed with esophageal cancer; of these, 387 males and 66 females were diagnosed with this cancer in the period 1993–97. In 165 patients (8.5%), esophageal cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of esophageal cancer was stable. In 1983–87, the crude incidence rate was 8.6/100,000 in males and 1.3/100,000 in females, whereas in 1993–97, it was 8/100,000 in males and 1.3/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 6%, i. e. from 83% to 89%. In the years 1993–97, the percentage of squamous cell carcinomas, adenocarcinomas, and non-differentiated cell carcinomas in the microscopically confirmed esophageal cancers was 81%, 8%, and 8%, respectively.

In the last observation period 1993–97, a higher percentage of elderly patients (Table 1) were included into the analysis and more patients with regional disease at diagnosis (Table 2).

In the period 1993–97, 60% of patients underwent specific treatment. In most cases, primary treatment was radiotherapy alone

TABELA 2: Požiralnik. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

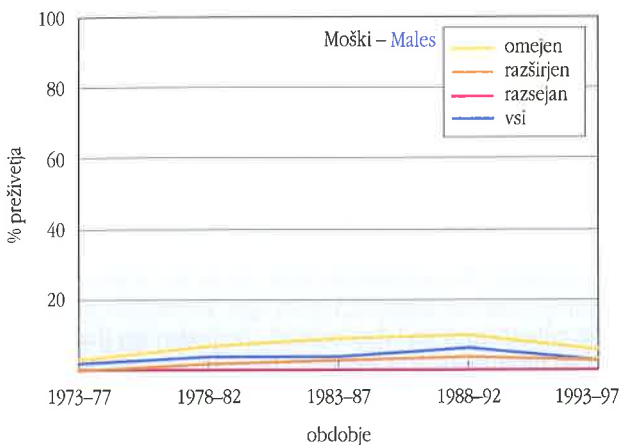
TABLE 2: Esophagus. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%				
Moški Males	1983-87 1988-92 1993-97	364 369 360	115 113 98	31,5 30,6 27,2	140 153 160	38,5 41,5 44,4	63 59 57	17,3 16,0 15,8	46 44 45	12,6 11,9 12,5
Ženske Females	1983-87 1988-92 1993-97	54 64 56	17 22 14	31,5 34,4 25,0	17 25 19	31,5 39,0 33,9	10 7 9	18,5 10,9 16,1	10 10 14	18,5 15,6 25,0

TABELA 3: Požiralnik. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Esophagus. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	19	(15-23)	4	(2-6)	3	(1-5)	21	(10-32)	10	(2-18)	6	(0-12)
1988-92	24	(20-28)	8	(5-11)	5	(3-7)	22	(12-32)	9	(2-16)	5	(1-9)
1993-97	23	(19-27)	3	(1-5)	3	(1-5)	27	(15-39)	13	(4-22)	13	(4-22)

Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	19	(15-23)	5	(2-8)	4	(2-6)	23	(11-35)	11	(1-21)	8	(1-15)
1988-92	25	(20-30)	9	(6-12)	6	(3-9)	23	(12-34)	11	(3-19)	6	(0-12)
1993-97	24	(19-29)	4	(2-6)	3	(0-4)	29	(16-42)	15	(4-26)	17	(5-29)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom požiralnika, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

Preživetje je bilo večje pri ženskah kot pri moških, pri slednjih pa največje v starosti 45-54 let.

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka požiralnika pri moških 8,6% (7,7-9,7) in pri ženskah 11% (9,7-12,4), v Sloveniji pa pri moških 5,5% (2,8-10,7) in pri ženskah 10,2% (4,6-22,8). Največje preživetje pri moških in pri ženskah je bilo v Španiji (samo na območju provinc: Baskija, Mallorca, Navarra in Tarragona): 12,9% oziroma 23%.

Miha Sok, Klinični oddelek za torakalno kirurgijo KC

Rak požiralnika je težko ozdravljiva bolezen. Zaradi obstrukcije požiralnika s tumorjem in težav s požiranjem bolnik skoraj vedno išče pomoč pri kirurgu.

Pogled iz klinične prakse potrjuje zbrane podatke: večina bolnikov ima ob diagnozi že razširjeno bolezen oziroma njihovo slabo splošno stanje in pridružene socialne bolezni preprečujejo

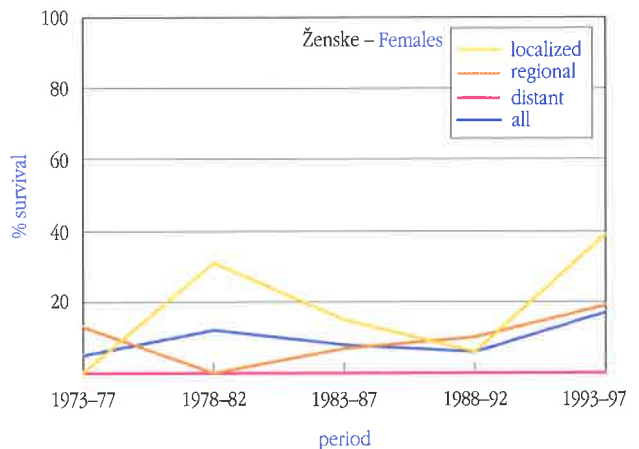
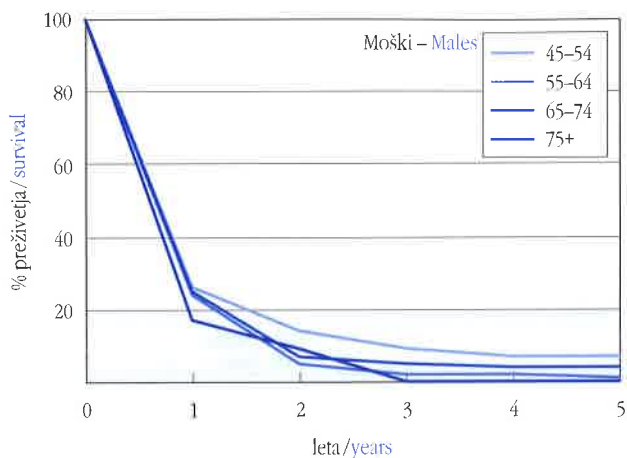


FIGURE 2: Relative five-year survival of esophageal cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

(38%) or surgery alone (36%) or combination of both. The patients were operated on at the Department of Thoracic Surgery, UMC in Ljubljana and in the General Hospitals in Maribor and in Celje, and they received radiotherapy at the Institute of Oncology in Ljubljana.

The relative five-year survival rate in the years 1993-97 was the same as in the years 1983-87, except that one-year survival increased by 5% (Figure 1). The survival was better in female patients than in male patients; in the latter, the highest survival was in the age group of 45-54 years.

According to the EURO CARE-3 study results for the period 1990-94, in Europe, the age-standardized relative survival rate of the patients with esophageal cancer was 8.6% (7.7-9.7) in male patients and in female patients 11% (9.7-12.4), while in Slovenia, it was 5.5% (2.8-10.7) in male patients and 10.2% (4.6-22.8) in female patients. The highest rates of 12.9% and of 23% were observed respectively in both sexes in Spain (only regions: Basque Country, Mallorca, Navarra and Tarragona).



SLIKA 3: Relativno petletno preživetje bolnikov z rakom požiralnika, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of esophageal cancer patients diagnosed in the period 1993–1997 by age.

aktivnejše zdravljenje. Polovico vseh bolnikov z novo odkritim rakom na požiralniku zdravimo simptomatsko ali naredimo omejen paliativni poseg, da omogočimo zadovoljivo prehranjevanje. Drugo polovico poskušamo radikalno operirati. Med njimi pa je le 20% s patološkim stadijem I in II, kjer je radikalno (kurativno) zdravljenje možno. Zato ne preseneča majhno petletno preživetje vseh bolnikov z rakom požiralnika.

Zgodnja diagnostika je že obrabljena fraza, ki pa še vedno drži, se pa zaradi socialne karakteristike tega raka ni izboljšala. Bolniki praviloma omalovažujejo težave in pridejo do zdravnika, ko je že prepozno.

Boris Jančar, Onkološki inštitut Ljubljana

Pred 3 leti smo bolnike z rakom požiralnika začeli zdraviti s kombiniranim zdravljenjem. Zdravljenje začnemo z obsevanjem in sočasno kemoterapijo, nato je bolnik operiran. Ocena uspešnosti tega zdravljenja še ni možna zaradi kratkega časa spremljanja, najverjetneje pa ne bo bistveno vplivala na celokupno preživetje, ker lahko tako zdravimo le majhen odstotek bolnikov (1).

VIR

1. Shrump DS, Altorki NK, Forastiere AA, Minsky BD. Cancer of the esophagus. In: deVita VT Jr, Hellman S, Rosenberg SA, editors. Cancer: principles and practice of oncology, 6th ed. Philadelphia: Lippincott, 2001: 1051–91.

Miha Sok, Department of Thoracic Surgery, UMC, Ljubljana

Esophageal cancer is a disease that is hard to manage. Because of the obstruction of the esophagus by tumor and the subsequent difficulties in swallowing, the patient almost always seeks help of a surgeon.

The collected data may certainly be supported by the experiences in clinical practice: in the majority of patients, the disease is advanced already at diagnosis. As the patients are usually in poor physical condition and additionally burdened with social diseases, aggressive treatment is not feasible. One half of the patients with newly detected esophageal cancer are therefore treated symptomatically or are given palliative therapy in order to facilitate the food intake. The other half of the patients undergoes radical surgery. Of these patients, only 20% have the stage I or II disease that allows radical (curative) treatment. A poor five-year survival of the patients with esophageal cancer is therefore far from being surprising.

Early detection is a saying that has become used out; but it still holds true. However, due to the social stigma attached to this disease, early diagnostics did not improve at all. The patients often ignore the symptoms and come to see the doctor when it is too late.

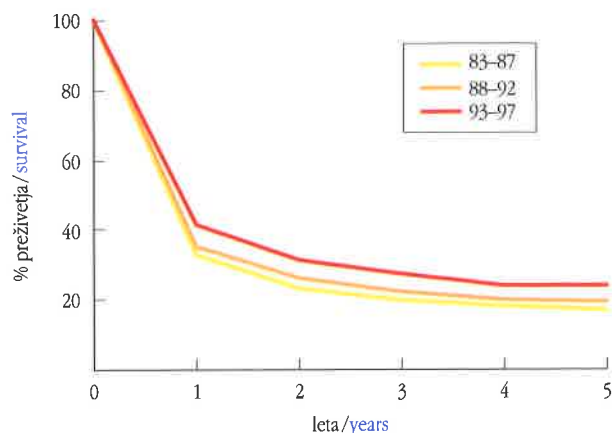
Boris Jančar, Institute of Oncology Ljubljana

The patients with esophageal cancer are treated with combined treatment that we initiated 3 years ago. We start the treatment with radiotherapy and concomitant chemotherapy that are followed by surgery. It is too early to make any assessment of this treatment regime because the patients have not been followed-up long enough. It is nevertheless expected that this treatment modality will not have any significant effect on the survival, as only a limited number of patients can receive it (1).

ŽELODEC

STOMACH

MKB 8/ICD 8: 151



SLIKA 1: Relativno petletno preživetje bolnikov z rakom želodca, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of stomach cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za želodčnim rakom 4695 moških in 3314 žensk, od tega v letih 1993–97 1568 moških in 1073 žensk. V analizo ni bilo vključenih 834 (10%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju je bila incidenca želodčne raka ustaljena. V letih 1983–87 je bila groba incidenčna stopnja 33,3/100.000 moških in 23,9/100.000 žensk, v letih 1993–97 pa 32,6/100.000 moških in 21/100.000 žensk. Odstotek mikroskopsko potrjenih primerov se je povečal z 81% v letih 1983–87 na 91% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 85% žlezni, 7% neopredeljenih karcinomov, 6% ne-Hodgkinovih limfomov in 0,6% leiomiosarkomov.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila, v zadnjih letih 1993–97 je bilo zajetih več starejših bolnikov (tabela 1). Razširjenost bolezni ob diagnozi se ni pomembno spremenila (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 56% bolnikov. Prvo zdravljenje je bilo v 83% samo kirurško, v 8% kirurško in citostatsko, v 4% samo citostatsko, v 2% kirurško, citostatsko in obsevalno in v 2% samo obsevalno. Bolniki so bili operirani na vseh kirurških oddelkih splošnih bolnišnic v Sloveniji, največ (38%) pa na Kliničnem oddelku za abdominalno

TABELA 1: Želodec. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Stomach. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi/Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	1379	0	72	186	363	423	335
Males	1988-92	1438	0	81	181	421	413	342
	1993-97	1432	2	75	152	404	478	321
Ženske	1983-87	1036	0	69	102	205	268	392
Females	1988-92	927	0	63	82	164	249	369
	1993-97	963	0	71	85	157	340	310

In the period 1983–97, a total of 4,695 male and 3,314 female patients were diagnosed with stomach cancer; of these, 1,568 males and 1,073 females were diagnosed with this cancer in the period 1993–97. In 834 patients (10%), stomach cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of this cancer was stable. In 1983–87, the crude incidence rate was 33.3/100,000 in males and 23.9/100,000 in females, whereas in 1993–97, it was 32.6/100,000 in males and 21/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 10%, i. e. from 81% to 91%. In the years 1993–97, the percentage of adenocarcinomas, non-differentiated cell carcinomas, non-Hodgkin lymphomas and leiomyosarcomas in the microscopically confirmed stomach cancers was 85%, 7%, 6% and 0.6%, respectively.

The age distribution of patients included into the analysis has changed. In the period 1993–97, the percentage of elderly patients was higher (Table 1). The stage distribution at diagnosis did not significantly change (Table 2).

In the period 1993–97, 56% of patients underwent specific treatment. Surgery alone was applied as primary treatment in 83%,

TABELA 2: Želodec. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

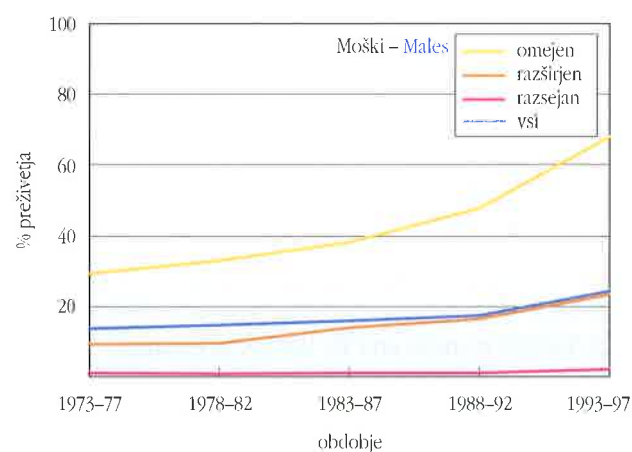
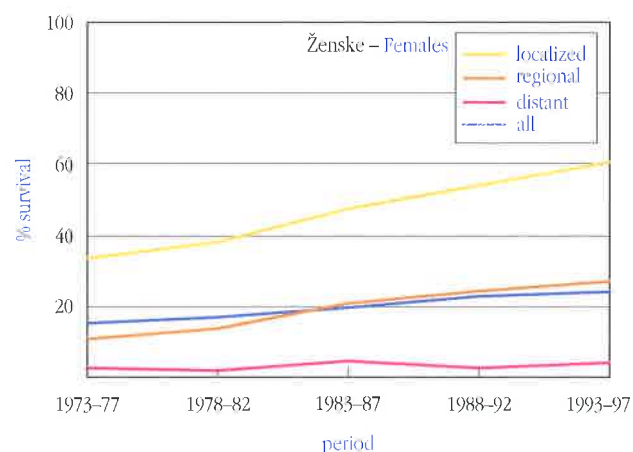
TABLE 2: Stomach. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij/Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%			
Moški	1983-87	1379	368	26,7	435	31,5	402	29,2	174	12,6
Males	1988-92	1438	318	22,1	479	33,3	469	32,6	172	12,0
	1993-97	1432	272	19,0	561	39,2	440	30,7	159	11,1
Ženske	1983-87	1036	236	22,8	287	27,7	334	32,2	179	17,3
Females	1988-92	927	218	23,5	305	32,9	261	28,2	143	15,4
	1993-97	963	214	22,2	333	34,6	283	29,4	133	13,8

TABELA 3: Želodec. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Stomach. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983–87	31	(29–33)	16	(14–18)	12	(10–14)	32	(29–35)	18	(16–20)	15	(13–17)
1988–92	32	(30–34)	18	(16–20)	13	(11–15)	37	(34–40)	22	(19–25)	18	(15–21)
1993–97	38	(35–41)	22	(20–24)	18	(16–20)	41	(38–44)	24	(21–27)	19	(16–22)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983–87	32	(29–35)	18	(16–20)	16	(14–18)	33	(30–36)	21	(18–24)	20	(17–23)
1988–92	34	(31–37)	21	(19–23)	17	(15–19)	38	(35–41)	25	(22–28)	23	(20–26)
1993–97	40	(37–43)	26	(23–29)	24	(21–27)	43	(40–46)	27	(24–30)	24	(21–27)

**SLIKA 2: Relativno petletno preživetje bolnikov z rakom želodca, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.****FIGURE 2: Relative five-year survival of stomach cancer patients diagnosed in the period 1973–1997 by stage and period of diagnosis.**

kirurgijo KC v Ljubljani. 10% bolnikov je pričelo zdravljenje na Onkološkem inštitutu v Ljubljani.

V letih 1993–97 je bilo relativno petletno preživetje za 7% večje kot v letih 1983–87 (slika 1), bolj pri moških kot pri ženskah (tabela 3). Preživetje se je povečalo pri bolnikih z omejeno in razširjeno boleznijo. Pri moških, mlajših od 45 let, je bilo za 31% večje kot pri starih 75 let in več (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za želodčnega raka pri moških 21,1% (20,4–21,9) in pri ženskah 26,5% (25,5–27,6), v Sloveniji pa pri moških 15,8% (13,5–18,4) in pri ženskah 19,1% (16,3–22,4). Največje preživetje pri moških je bilo 31,2% na Islandiji in pri ženskah 37,5% na Tirolskem v Avstriji.

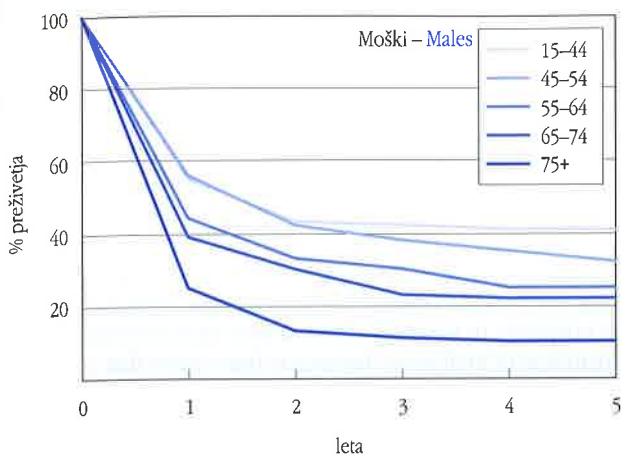
Stane Repše, Klinični oddelek za abdominalno kirurgijo KC

V diagnostiki želodčnega raka je v začetku 80. let endoskopska preiskava z biopsijami sumljivih sprememb na sluznici

8% were treated with surgery and chemotherapy, 4% with chemotherapy alone, 2% with combination of surgery, chemotherapy and radiotherapy, and 2% with radiotherapy alone. The patients underwent surgery at surgical departments of all 11 general hospitals in Slovenia. The highest percentage (38%) of patients was operated on at the Department of Abdominal Surgery, UMC in Ljubljana. Primary treatment was started at the Institute of Oncology Ljubljana in 10% of patients.

The relative five-year survival rate in the years 1993–97 was 7% higher than in the years 1983–87 (Figure 1). The survival was better in female patients than in male patients (Table 3). The survival improved in the patients with localized and regional disease. In males below 45 years of age, it was 31% higher than in those older than 75 years (Figure 3).

According to the EURO CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with stomach cancer was 21.1% (20.4–21.9) in male patients and in female patients 26.5% (25.5–27.6), while in Slovenia, it was 15.8% (13.5–18.4) in male patients and 19.1



SLIKA 3: Relativno petletno preživetje bolnikov z želodčnim rakom, zbolelih v letih 1993–1997 po starosti.

prevzela vodilno vlogo. Za predoperativno zamejitev bolezni se je sredi 80. let uveljavil klasični ultrazvok in sredi 90. endoskopski ultrazvok. Patologi so v 80. letih dodatno standardizirali analize resektatov z Laurenovo histološko klasifikacijo želodčnega raka, stopnjo malignosti (G) in UICC pTNM ter v 90. še z R klasifikacijo.

Do začetka 80. let je bil princip kirurškega zdravljenja želodčnega raka resekcija z omentektomijo (distalna subtotalna resekcija iz principa, totalna gastrektomija iz nuje). V 1982. letu je bila uvedena nova strategija – načrtovanje operacije v odvisnosti od histološkega tipa (Lauren), od lokacije raka na želodcu (tretjine) in od globine infiltracije (T) ter v 1986. letu sistematična limfadenektomija I. in II. skupine bezgavk – D2 (1). Delež totalnih gastrektomij se je postopoma dvignil od 5–10% na 30–40% (2).

V prvi polovici 90. let je multidisciplinarna skupina strokovnjakov izdelala »Priporočila za celostno obravnavo bolnikov z rakom prebavil«. Sprejela so jih vsa strokovna telesa, potrdil jih je Zdravstveni svet pri Ministrstvu za zdravstvo Republike Slovenije. Izšla so v knjižni obliki in postala dostopna vsem zdravnikom v Sloveniji (3).

V 1995. letu sta dve kirurški delavnici in simpozija ter Zbornik »Kirurgija želodca« pripomogli, da so to strategijo postopoma prevzeli tudi drugi kirurški oddelki (1).

Čeprav je radikalna operacija edina metoda, ki nudi možnost ozdravitve, kar tretjina novo odkritih bolnikov z želodčnim rakom v tem obdobju sploh ni prišla do kirurškega oddelka. V letu 1993 je bilo na vseh kirurških oddelkih zdravljenih samo 72% (374/520) novo odkritih primerov v tem letu in v letu 2000 samo 69% (330/480) (1). Vzroki za to niso pojasnjeni, gotovo pa to prispeva k nizkemu 5-letnemu preživetju bolnikov z želodčnim rakom v državi.

V opazovanem obdobju je bila poprečno vsa leta tretjina bolnikov operiranih v KC v Ljubljani, tretjina v dveh večjih regionalnih bolnišnicah in tretjina v preostalih bolnišnicah. V začetku 90. let se je začelo močno poudarjati, da je zdravljenje malignih bolezni v centrih, ki imajo kritično število bolnikov (high

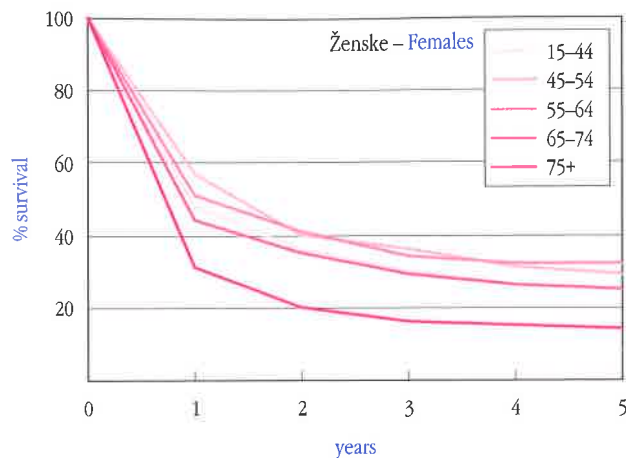


FIGURE 3: Relative five-year survival of stomach cancer patients diagnosed in the period 1993–1997 by age.

(16.3–22.4) in female patients. The highest rates of 31.2% and of 37.5% were observed respectively in male patients in Iceland and in female patients in Tyrol in Austria.

Stane Repše, Department of Abdominal Surgery, UMC, Ljubljana

Endoscopic examination and biopsy of suspicious changes of the mucous membrane took on the leading role in the diagnostics of stomach cancer in early 1980s. In preoperative disease staging, standard ultrasonography was introduced in the mid-1980s, whereas endoscopic ultrasonography came into use in the mid-1990s. In the 1980s, pathologists additionally standardized the analyses of resections by Lauren's histology classification for stomach cancer, malignancy stage (G) and UICC pTNM, and in the 1990s, also by R classification.

Until the early 1980s, the principal surgical treatment of stomach cancer involved resection with omentectomy (in principle, distal subtotal resection, total gastrectomy when otherwise not possible). A new strategy was initiated in 1982 that implied surgery planning depending upon the histology type (Lauren), subsite (thirds of the stomach), and depth of infiltration (T). In 1986, systemic lymphadenectomy of the groups of lymph nodes I and II – D2 was initiated (1). The proportion of total gastrectomies was gradually increasing from 5–10% to 30–40% (2).

In the first half of the 1990s, a multidisciplinary team of experts elaborated »Recommendations for a Comprehensive Approach to Patients with Digestive Cancer«. These recommendations were adopted by all professional boards and approved by the Health Council at the Ministry of Health of the Republic of Slovenia. They were published as a booklet and thus made available to all Slovenian physicians (3).

In 1995, two workshops and symposia on surgery with the proceedings »Stomach Surgery« facilitated the implementation of this strategy also in the surgical departments of other hospitals (1). Though radical surgery is the sole treatment modal-

volume), bistveno uspešnejše. V zadnjih letih je tudi pri nas vse večji delež bolnikov operiran na večjih oddelkih. Manjši kirurški oddelki skoraj ne operirajo več bolnikov z želodčnim rakom (3).

Prizadevanja zadnjih 20. let za lažjo dostopnost endoskopskih preiskav, za spremljanje skupin bolnikov z visokim tveganjem, za multidisciplinarno obravnavo bolnikov, za standardizirano kirurško zdravljenje na večjih kirurških oddelkih ter za specifično onkološko zdravljenje se bodo pokazala z boljšimi rezultati zdravljenja na nacionalnem nivoju v naslednjem obdobju (3).

VIRI

1. Repše S, Juvan R. Kirurgija raka želodca v Sloveniji. In: Repše S ed. Kirurgija želodca: kirurška šola. Ljubljana: Kirurške klinike KC, 1995; 101–12.
2. Repše S, Jelenc F, Žakelj B et al. Rak želodca – spremembe v naši patologiji v dveh desetletjih. Zdrav Vestn 1991; 60: 281–5.
3. Anon. Rak želodca. In: Repše S ed. Priporočila za celostno obravnavo bolnikov z rakom prebavil. Ljubljana: Ministrstvo za zdravstvo R Slovenije, 1997; 13–21.

ity that offers the possibility of cure, about one third of patients with newly detected stomach cancer have never entered a surgical unit in this period. In 1993, only 72% (374/520) of patients with newly detected stomach cancer were treated at various surgical units, whereas in 2000, only 69% (330/480) (1). No explanation has ever been given for such circumstances, though they definitely contribute to a poor five-year survival of patients with stomach cancer in Slovenia.

In the observed period, on average one third of patients was operated on in UMC in Ljubljana, the other third in two major regional hospitals and the last third in the remaining general hospitals. In the early 1990s, it was often stressed that the treatment of malignant diseases in the centers that can admit a critical number of patients is significantly more effective. In recent years, an increasing proportion of patients are operated on at larger departments of major hospitals in Slovenia. In minor surgical departments, they practically do not operate any more the patients with stomach cancer (3).

The benefits of our twenty-year endeavors to facilitate the access to endoscopic examinations, follow-up of high-risk patients, multidisciplinary approach to patients, standardized surgical treatment at major surgical units and at specialized cancer treatment departments will start to have an impact on the treatment results on the national level only in the next observation period (3).

DEBELO ČREVO

COLON

MKB 8 / ICD 8: 153

V obdobju 1983–97 je zbolelo za rakom debelega črevesa 2694 moških in 2819 žensk, od tega v letih 1993–97 1175 moških in 1187 žensk. V analizo ni bilo vključenih 375 (7%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka debelega črevesa večala. V letih 1983–87 je bila groba incidenčna stopnja 12,9/100.000 moških in 14,8/100.000 žensk, v letih 1993–97 pa 24,4/100.000 moških in 23,2/100.000 žensk. Odstotek mikroskopsko potrjenih primerov se je povečal s 84% v letih 1983–87 na 92% v letih 1993–97.

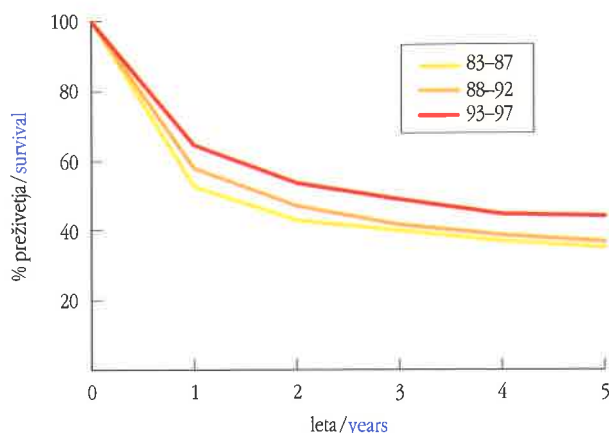
Starostna porazdelitev v analizo zajetih bolnikov se ni spremenila (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila. V letih 1993–97 je bilo ob natančnejši diagnostiki ugotovljeno več bolezni z regionalno razširitvijo (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 81% bolnikov. Prvo zdravljenje je bilo v 74% samo kirurško, v 15% je bila operaciji dodana kemo- in imunoterapija, v 9% samo kemoterapija, obsevan je bil le dober odstotek bolnikov. V letih 1988–92 je bilo specifično zdravljenih 77% bolnikov: samo kirurško 69%, 12% je dobilo še kemoterapijo, 7% kemo- in imunoterapijo, obsevani so bili 4%, za 8% pa način zdravljenja Registru ni bil sporočen (verjetno so bili operirani). Ope-

TABELA 1: Debelo črevo. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Colon. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	558	2	31	72	126	189	138
Males	1988-92	859	1	50	108	235	244	221
	1993-97	1109	1	51	122	311	392	232
Ženske	1983-87	670	1	28	70	165	210	196
Females	1988-92	833	0	48	83	176	247	279
	1993-97	1109	1	49	111	241	361	346



SLIKA 1: Relativno petletno preživetje bolnikov z rakom debelega črevesa, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of colon cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 2,694 male and 2,819 female patients were diagnosed with colon cancer; of these, 1,175 males and 1,187 females were diagnosed with this cancer in the period 1993–97. In 375 patients (7%), this cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of colon cancer was increasing and so did mortality. In 1983–87, the crude incidence rate was 12.9/100,000 in males and 14.8/100,000 in females, whereas in 1993–97, it was 24.4/100,000 in males and 23.2/100,000 in females. In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 8%, i. e. from 84% to 92%.

The age distribution of patients included into the analysis has not changed (Table 1), whereas the stage distribution at diagnosis has. In the last observation period 1993–97, a higher percentage of patients with regional disease was observed (Table 2).

In the period 1993–97, 81% of patients underwent specific treatment. Surgery alone was performed as primary treatment in 74% of patients, in 15% of patients, postoperative adjuvant chemotherapy and immunotherapy were applied, 9% received chemotherapy alone, and 1% radiotherapy alone.

TABELA 2: Debelo črevo. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

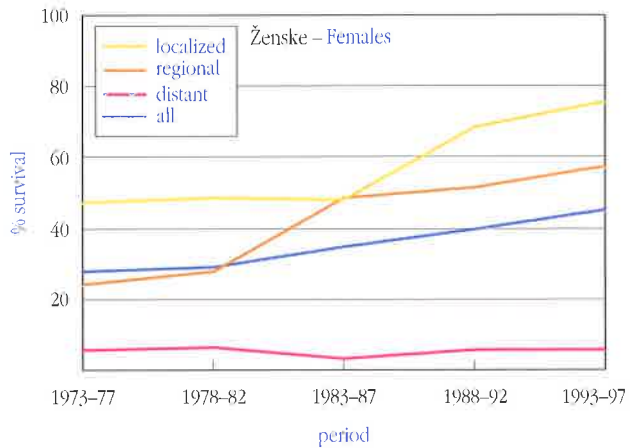
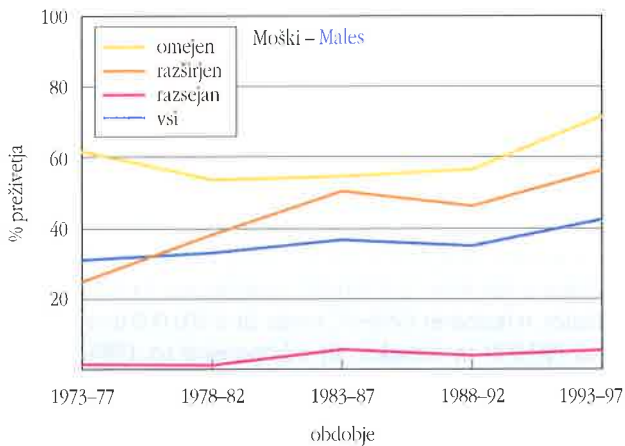
TABLE 2: Colon. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij / Stage							
			Omejen/ Localized	%	Razširjen/ Regional	%	Razsejan/ Distant	%	Neznan/ Unknown	%
Moški	1983-87	558	99	17,7	265	47,5	146	26,2	48	8,6
Males	1988-92	859	124	14,4	443	51,6	215	25,0	77	9,0
	1993-97	1109	125	11,3	599	54,0	319	28,8	66	6,0
Ženske	1983-87	670	139	20,7	316	47,2	156	23,3	59	8,8
Females	1988-92	833	118	14,2	440	52,8	200	24,0	75	9,0
	1993-97	1109	136	12,3	640	57,7	251	22,6	82	7,4

TABELA 3: Debelo črevo. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Colon. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	48	(44-52)	34	(30-38)	28	(24-32)	52	(48-56)	35	(31-39)	28	(25-31)
1988-92	55	(52-58)	34	(31-37)	27	(24-30)	56	(53-59)	38	(35-41)	32	(29-35)
1993-97	60	(57-63)	41	(38-44)	32	(29-35)	63	(60-66)	44	(41-47)	36	(33-39)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	51	(46-56)	41	(36-46)	36	(31-41)	54	(50-58)	39	(35-43)	35	(31-39)
1988-92	58	(54-62)	40	(36-44)	35	(31-39)	58	(54-62)	43	(39-47)	40	(36-44)
1993-97	63	(60-66)	48	(45-51)	42	(38-46)	66	(63-69)	50	(47-53)	45	(42-48)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom debelega črevesa, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

FIGURE 2: Relative five-year survival of colon cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

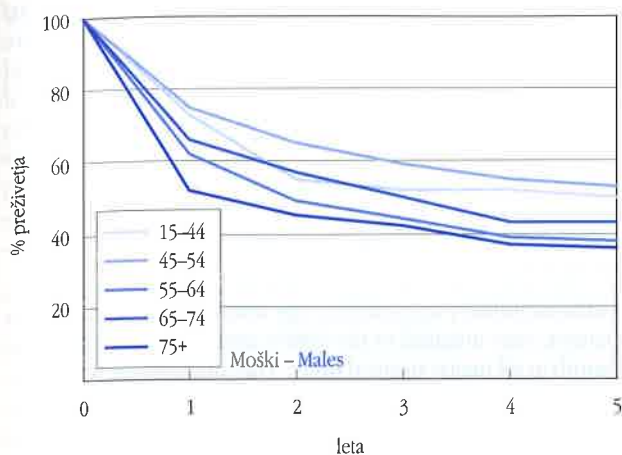
rirani so bili na vseh kirurških oddelkih splošnih bolnišnic v Sloveniji, v letih 1993-97 največ (41%) na Kliničnem oddelku za abdominalno kirurgijo KC v Ljubljani. 5% bolnikov pa je pričelo zdravljenje na Onkološkem inštitutu v Ljubljani.

V letih 1993-97 je bilo relativno petletno preživetje za 9% večje kot v letih 1983-87 (slika 1), bolj pri moških kot pri ženskah (tabela 3). Preživetje se je povečalo pri bolnikih z omejeno in razširjeno boleznijo. Pri moških, mlajših od 55 let je bilo za 20% večje kot pri starih 65 let in več, pri ženskah so bile razlike po starosti še večje (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka debelega črevesa pri moških 50% (49,1-50,9) in pri ženskah 51,9% (51,1-52,8), v Sloveniji pa pri moških 36,3% (32,5-40,5) in pri ženskah 39,8% (36,2-43,8). Največje preživetje pri moških in pri ženskah je bilo v treh okrožjih Francije (Bas-Rhin, Calvados in Cote d'Or): 57,2% oziroma 60,1%.

In the period 1988-92, 77% of patients underwent specific treatment. Surgery alone was performed in 69% of patients, in 12% of patients, postoperative chemotherapy was applied, 7% of patients were treated with chemotherapy and immunotherapy, 4% received radiotherapy alone, whereas the treatment modality applied in 8% of patients was never reported to the Registry (it is assumed that they were operated on). Surgical treatment of these patients was carried out at the surgical departments of all general hospitals in Slovenia; in the period 1993-97, the majority of patients (41%) was operated on at the Department of Abdominal Surgery, UMC in Ljubljana; 5% of patients received primary treatment at the Institute of Oncology, Ljubljana.

The relative five-year survival rate was 9% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The survival increased in males as well as in females (Table 3), and in the patients with localized and regional disease. In the males under the age of 55, the survival was 20% higher than in those over 65 years. In females, the differences in survival with regard to the age of patients were even bigger (Figure 3).



SLIKA 3: Relativno petletno preživetje bolnikov z rakom debelega črevesa, zbolelih v letih 1993–1997 po starosti.

Stane Repše, Klinični oddelek za abdominalno kirurgijo KC

Presejanja prebivalstva zaradi raka debelega črevesa in danke v Sloveniji še ni. Kolonoskopija z biopsijami sumljivih sprememb je bila že sredi 80. let priporočena diagnostična metoda, vendar je bila, zaradi premajhnih zmogljivosti endoskopije na nacionalnem nivoju, rentgenska diagnostika z irigografijo še pogosto prva ali celo edina preiskava (v letu 1995 še pri 18% vseh bolnikov z rakom debelega črevesa in danke v Sloveniji) (1). Za predoperativno zamejitev bolezni so se v tem obdobju uveljavile slikovne diagnostike; v 80. letih klasičen ultrazvok in računalniška tomografija, v 90. letih pa endoskopski ultrazvok in deloma MRI. Patologi so standardizirali analize resektatov z določanjem stopnje malignosti (G), UICC pTNM in R klasifikacijo, kar je omogočilo odločanje o dodatnem onkološkem zdravljenju, boljše napovedovanje prognoze, raziskovalno delo in primerjave lastnih rezultatov zdravljenja z drugimi.

Bolnike z rakom debelega črevesa so v obdobju 1983–1997 operirali na vseh kirurških oddelkih v Sloveniji, kjer je bilo hospitaliziranih 90–95% vseh bolnikov z rakom debelega črevesa. V KC v Ljubljani je bilo zdravljenih 40–45% bolnikov, v dveh večjih regionalnih bolnišnicah četrtna in tretjina v preostalih bolnišnicah (1).

Princip kirurškega zdravljenja raka debelega črevesa je bil v tem obdobju radikalna resekcija. Ob koncu 80. let se je začela uvajati radikalnejša kirurgija raka debelega črevesa; tipične standardne radikalne in razširjene radikalne resekcije z radikularnim ligiranjem področnih žil z limfadenektomijo. Dve kirurški delavnici in simpozija »Kirurgija širokega črevesa in danke« v letu 1996 ter Zbornik »Kirurgija širokega črevesa in danke« so pripomogli k širjenju radikalnejše kirurgije tudi na druge kirurške oddelke v Sloveniji (1).

Multidisciplinarno obravnavanje bolnikov se je v 80. letih začelo uveljavljati in v 90. letih postalo na večjih oddelkih tudi pravilo. K temu so pripomogli seminarji ob začetku vseslovenske študije o raku debelega črevesa in publikacija »Adjuvantno

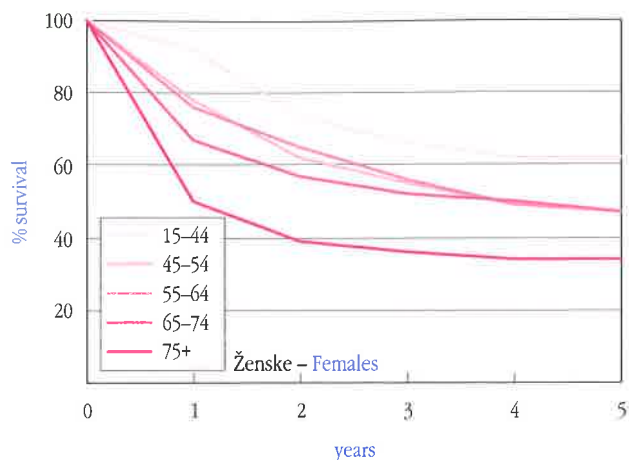


FIGURE 3: Relative five-year survival of colon cancer patients diagnosed in the period 1993–1997 by age.

According to the EURO-CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with colon cancer was 50% (49.1–50.9) in male patients and in female patients 51.9% (51.1–52.8), while in Slovenia, it was 36.3% (32.5–40.5) in male patients and 39.8% (36.2–43.8) in female patients. The highest rates of 57.2% and of 60.1% were observed respectively in both sexes in three regions in France: Bas-Rhin, Calvados and Cote d'Or.

Stane Repše, Department of Abdominal Surgery, UMC, Ljubljana

In Slovenia, no screening for colorectal cancer has been so far started. Since the 1980s, the methods recommended in the diagnostics of this cancer have been colonoscopy and biopsy; however, due to the limited potentials of endoscopy at the national level, X-ray diagnostics with irigography was often the method of choice or, in some cases, the only one (e. g. in 1995, in as much as 18% of patients with colorectal cancer) (1). The preoperative staging of the disease was then based on imaging diagnostics, viz. classic ultrasonography and computer tomography in the 1980s, and in the 1990s, endoscopic ultrasonography and partly also magnetic resonance imaging. Pathologists standardized the analyses of resections by determining the malignancy grade (G) according to UICC pTNM and R classifications. Both classifications facilitated the decisions with respect to the application of adjuvant cancer therapy, better prognostication of the disease and research together with the comparison of our own treatment results with the results of other studies.

In the years 1983–1997, the patients with colon cancer were surgically treated at surgical departments of all general hospitals in Slovenia. Of 90–95% of colon cancer patients who were hospitalized at that period in Slovenia, 40–45% were admitted to treatment at UMC in Ljubljana. One fourth was treated at two major county hospitals and one third in the remaining Slovenian hospitals (1).

zdravljenje bolnikov z operabilnim rakom debelega črevesa* (2). Adjuvantno in paliativno onkološko zdravljenje, ki je bilo v opazovanem obdobju na nacionalnem nivoju sprva fakultativno, je v 90. letih postalo standard (3).

Za 9% boljše relativno 5-letno preživetje bolnikov na nacionalnem nivoju v obdobju 1993–97 v primerjavi z obdobjem 1983–87 je posledica nekoliko hitrejše diagnostike zaradi lažje dostopnosti endoskopskih preiskav, uvajanja sodobnih principov operacijskega zdravljenja na večini kirurških oddelkov, boljšega pooperacijskega in specifičnega onkološkega zdravljenja.

Zanimivo je, da je v tem obdobju kar za 6% padel delež lokalizirane bolezni na debelem črevesu pri moških in za 8% pri ženskah in se za toliko dvignil delež bolnikov z regionalno (bolj napredovano) boleznijo. Delež bolnikov z oddaljenimi zasevki je v tem obdobju porasel za 2% pri moških in pri ženskah padel za 1% (tabela 2). To kaže na boljše zamejevanje bolezni pred operacijo zaradi rutinske rabe natančnejših preiskovalnih metod (ultrazvok, računalniška tomografija), med operacijo (intraoperativni ultrazvok) in na standardizirano definitivno patološko zamejitev bolezni na reseciranim preparatu.

Prizadevanja zadnjih 15 let za multidisciplinarno obravnavo bolnikov, za lažjo dostopnost do endoskopskih preiskav, za preventivne preglede skupin z visokim tveganjem in endoskopsko odstranjevanje preneoplastičnih lezij, za standardizirano kirurško zdravljenje samo na večjih kirurških oddelkih, za specifično onkološko zdravljenje in sledenje reseciranih bolnikov bodo pokazala boljše rezultate zdravljenja na nacionalnem nivoju v naslednjem obdobju (2).

Borut Štabuc, Klinični oddelek za gastroenterologijo KC

Delež omejene bolezni je bil v zadnjem obdobju manjši zaradi natančnejšega določanja stadija. Večje preživetje bolnikov z omejeno in razširjeno boleznijo je v prvi vrsti posledica standardizacije operacij ter standardne dopolnilne kemoterapije po evropskih in ameriških priporočilih. Skupno preživetje se je v manjši meri povečalo tudi zaradi skrbnejšega nadzora bolnikov po zaključenem zdravljenju, zgodnjega odkrivanja resektabilnih zasevkov in metahronega črevesnega raka ter zaradi specifičnega onkološkega zdravljenja bolnikov z razširjeno boleznijo.

Petletno preživetje bolnikov z operabilnim rakom debelega črevesa je v primerjavi z nekaterimi evropskimi državami manjše zaradi večjega deleža bolnikov z večjim primarnim tumorjem in večjim številom pozitivnih bezgavk (4). V Sloveniji smo po letu 1993 standardizirali operacije, histopatološke preglede resektatov in uvedli doktrinarno dopolnilno zdravljenje. Izvajamo aktivno pooperativno sledenje zaradi čimprejšnjega kurativnega in sodobnega paliativnega zdravljenja.

Preživetje bolnikov pa lahko pomembno izboljšamo le z zgodnjim odkrivanjem te bolezni.

At that time, radical resection was considered as standard surgical treatment of colon cancer. In the late 1980s, even more radical resection was introduced, *viz.* standard radical and more extensive radical resections with radical ligature of regional blood vessels including lymphadenectomy. Two workshops and symposia on the surgery of the colon and rectum held in 1996 and the proceedings »Surgery of the colon and rectum« had an influential role in promoting a more radical surgery of the colon and rectum at other surgical departments (1).

Multidisciplinary approach to the treatment of colon cancer patients was initiated in the 1980's and became a rule of the thumb at all major surgical units. This step further was largely due to the seminars that were held at the very start of a comprehensive Slovenian study on colon cancer and the publication »Adjuvant treatment of the patients with operable cancer of the colon« (2). Adjuvant and palliative cancer treatments, which were, at the national level, applied facultatively in the 1980's, became a standard treatment in the 1990s (3).

In comparison to the five-year survival rate at the national level in 1983–87, an increase of 9% was observed in the period 1993–97 that is attributable to a more rapid and precise diagnostics facilitated by easier availability and accessibility of endoscopic examinations, to the introduction of most recent standards of surgical treatment at the majority of surgical departments in Slovenia, and to the improved postoperative and specific cancer treatment.

It is interesting that the percentage of localized colon cancer declined in males and females by 6% and 8%, respectively, and that regional disease increased by the same percentages in both sexes. The percentage of the patients with distant metastases increased by 2% in males and dropped by 1% in females (Table 2). This may prove that the disease staging has become more advanced: the preoperative staging by the routine use of more precise examination methods (ultrasonography, computer tomography), the intraoperative staging by intraoperative ultrasonography, as well as postoperative staging by the standardization of pathology staging of the disease on the resected sample.

The recent 15 years of best endeavors were aimed to enhance the multidisciplinary approach to the treatment of patients, to facilitate the access to preventive endoscopic examination in high-risk groups of patients and as an endoscopic means for removing preneoplastic lesions, to standardize surgical treatment only at major surgical departments, to further develop specific cancer treatment and to follow-up the patients after surgery. All these endeavors will give better treatment results at the national level not until the next observation period (2).

Borut Štabuc, Department of Gastroenterology, UMC

The percentage of localized disease in the last observation period dropped because of the progressively more precise disease staging. Better survival of the patients with localized and regional disease is in the first place due to the standardization of surgical treatment and of adjuvant chemotherapy in

VIRI

1. Repše S, Štor Z, Juvan R. Kirurgija raka širokega črevesa in danke v Sloveniji. In: Repše S, ed. Kirurgija širokega črevesa in danke: kirurška šola. Ljubljana: Kirurške klinike KC 1996; 118–26.
2. Štabuc B, Zakotnik B, Markovič S, Repše S, Benulič T, Golouh R: Adjuvantno zdravljenje bolnikov z operabilnim rakom debelega črevesa. OIGIT-01/02-92. Ljubljana: Onkološki inštitut, 1992.
3. Markovič S in sod. Rak širokega črevesa in danke. In: Repše S, ed. Priporočila za celostno obravnavo bolnikov z rakom prebavil. Ljubljana: Ministrstvo za zdravstvo R Slovenije, 1997; 23–32.
4. Anon. Differences in the survival of colorectal cancer patients between Europe and USA. Final report. Agreement No. S12.117414. Milano, 2001.

accordance with the European and American recommendations. The increase of overall survival rate may also be attributed to a more careful follow-up of patients after completed treatment, to early detection of resectable metastases and of metachronous colon cancer and to a specific cancer treatment of the patients with regional disease.

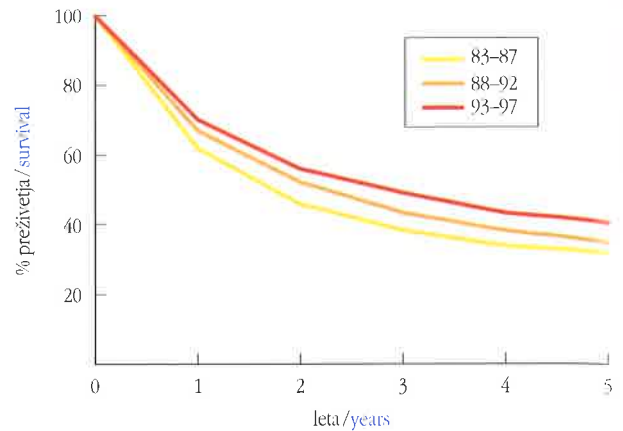
Five-year survival rate of the patients with operable cancer of the colon is worse in Slovenia than in other European countries. This is mainly due to the higher percentage of the patients with larger primary tumor and with larger number of positive lymph nodes (4). After 1993, standardization of surgical treatment and of histologic examination of resected samples and guidelines for adjuvant treatment were elaborated and put into practice. We are carefully following up the patients after surgical treatment in order to apply curative or palliative treatment when it is appropriate.

The survival may only be improved by earlier detection of the disease.

DANKA

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SLIKA 1: Relativno petletno preživetje bolnikov z rakom danke, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of rectal cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom danke 3062 moških in 2687 žensk, od tega v letih 1993–97 1214 moških in 1012 žensk. V analizo ni bilo vključenih 325 (6%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka danke večala. Tudi umrljivost se je še večala. V letih 1983–87 je bila groba incidenčna stopnja 18,2/100.000 moških in 16,1/100.000 žensk, v letih 1993–1997 pa 25,2/100.000 moških in 19,8/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal z 88% v letih 1983–87 na 93% v letih 1993–97.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila, v letih 1993–97 je bilo zajetih več starejših bolnikov (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila. V zadnjem obdobju je bilo ob natančnejši diagnostiki ugotovljeno več bolezni z regionalno razširitvijo (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 80% bolnikov, od teh največ samo kirurško (53%). Kombinirano z operacijo, obsevanjem in kemoterapijo je bilo zdravljenih 15%, samo z operacijo in obsevanjem 10%, z operacijo, kemo-, imuno-terapijo in obsevanjem 8%, samo z obsevanjem 5%, z opera-

In the period 1983–97, a total of 3,062 male and 2,687 female patients were diagnosed with rectal cancer; of these, 1,214 males and 1,012 females were diagnosed with this cancer in the period 1993–97. In 325 patients (6%), rectal cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of rectal cancer was increasing. The mortality rate was increasing, too. In 1983–87, the crude incidence rate was 18.2/100,000 in males and 16.1/100,000 in females, whereas in 1993–97, it was 25.2/100,000 in males and 19.8/100,000 in females. In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 5%, i. e. from 88% to 93%.

The age distribution of patients included into the analysis changed. In the period 1993–97, a higher percentage of elderly patients were included into the analysis (Table 1). The stage distribution of the disease at diagnosis changed, too. In the last observation period 1993–97, a higher percentage of patients with regional disease was observed (Table 2).

In the period 1993–97, 80% of patients underwent specific treatment. Surgery alone was performed in 53% of patients, 15% of patients, received combined treatment consisting of radio-

TABELA 1: Danka. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Rectum. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški Males	1983-87	802	0	45	123	190	228	216
	1988-92	946	0	40	128	315	240	223
	1993-97	1169	0	41	140	361	388	239
Ženske Females	1983-87	745	0	43	71	170	232	229
	1988-92	813	0	32	72	202	242	265
	1993-97	949	0	48	95	210	341	255

TABELA 2: Danka. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

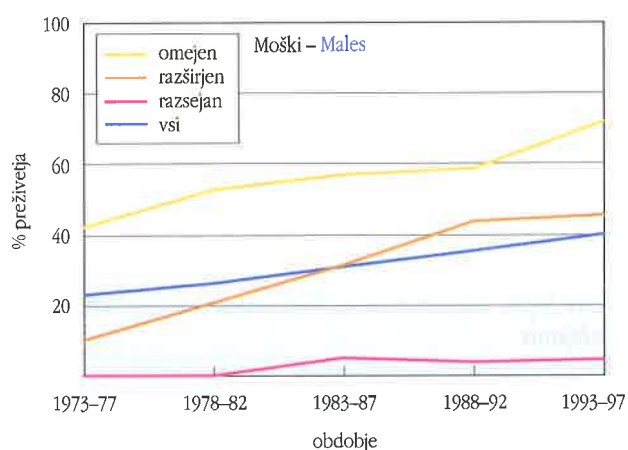
TABLE 2: Rectum. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij / Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown				
Moški Males	1983-87	802	179	22,3	384	47,9	166	20,7	73	9,1
	1988-92	946	160	16,9	475	50,2	220	23,3	91	9,6
	1993-97	1169	209	17,9	622	53,2	232	19,8	106	9,1
Ženske Females	1983-87	745	179	24,0	355	47,7	125	16,8	86	11,5
	1988-92	813	150	18,5	427	52,5	150	18,5	86	10,6
	1993-97	949	184	19,4	484	51,0	177	18,7	104	11,0

TABELA 3: Danka. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Rectum. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	59	(55-63)	31	(28-34)	23	(20-26)	60	(56-64)	34	(31-37)	27	(24-30)
1988-92	64	(61-67)	37	(34-40)	27	(24-30)	63	(60-66)	38	(35-41)	28	(25-31)
1993-97	67	(64-70)	42	(39-45)	31	(28-34)	67	(64-70)	44	(41-47)	35	(32-38)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	62	(58-66)	37	(33-41)	31	(27-35)	62	(58-66)	38	(34-42)	33	(29-37)
1988-92	67	(64-70)	43	(39-47)	35	(31-39)	65	(61-69)	42	(38-46)	35	(31-39)
1993-97	71	(68-74)	48	(45-51)	40	(36-44)	70	(67-73)	49	(45-53)	43	(39-47)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom danke, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

cijo, kemo- in imunoterapijo 3%, z obsevanjem in kemoterapijo 3% in z operacijo in kemoterapijo 2%. Operirani so bili na vseh kirurških oddelkih splošnih bolnišnic v Sloveniji, največ (36%) pa na Kliničnem oddelku za abdominalno kirurgijo KC v Ljubljani. 13% bolnikov je pričelo zdravljenje na Onkološkem inštitutu v Ljubljani.

V letih 1993-97 je bilo relativno petletno preživetje za 9% večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo pri bolnikih z omejeno in razširjeno boleznijo. Preživetje je bilo največje pri moških, starih 55-64 let (za 30% večje kot pri starih 75 let in več), pri ženskah pa v starosti do 44 let (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka danke pri moških 45,7% (44,6-46,8) in pri ženskah 50,2% (49,1-51,4), v Sloveniji pa pri moških 34% (30,3-38) in pri ženskah 35,2% (31,7-39,2). Največje preživetje pri moških je bilo 55,8% v Švici na območju registrov iz Basla in Ženeve in pri ženskah 63,4% v Franciji (Bas-Rhin, Calvados in Cote d'Or).

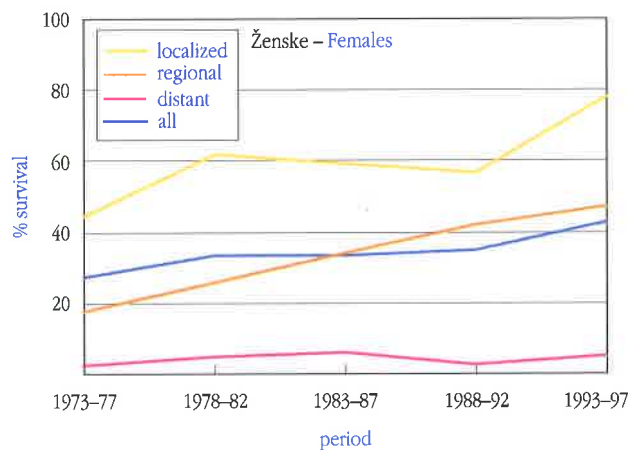
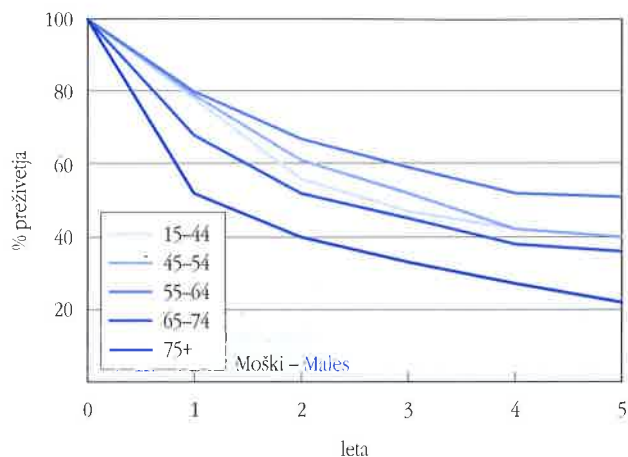


FIGURE 2: Relative five-year survival of rectal cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

therapy, surgery and chemotherapy, 10% were treated with radiotherapy and surgery, 8% received radiotherapy, surgery, chemo- and immunotherapy, 5% radiotherapy alone, 3% radio- and chemotherapy, 3% surgery, chemo- and immunotherapy, and 2% surgery and chemotherapy. Surgical treatment of these patients was carried out at the surgical departments of all general hospitals in Slovenia; the majority of patients (36%) was operated on at the Department of Abdominal Surgery of UMC in Ljubljana; 13% of patients received primary treatment at the Institute of Oncology, in Ljubljana.

The relative five-year survival rate was 9% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The survival increased in the patients with local and in those with regional disease and was the highest in the males aged between 55-64 years (30% higher than in the patients over 75 years). The survival of the female patients was the highest in the age group up to 44 years (Figure 3).

According to the EURO CARE-3 study results for the period 1990-94, in Europe, the age-standardized relative survival rate of the patients with rectal cancer was 45.7% (44.6-46.8)



SLIKA 3: Relativno petletno preživetje bolnikov z rakom danke, zbolelih v letih 1993–1997 po starosti.

Stane Repše, Klinični oddelek za abdominalno kirurgijo KC

Presejanja prebivalstva zaradi raka debelega črevesa in danke v Sloveniji še ni. Kolonoskopija z biopsijami sumljivih sprememb je bila že sredi 80. let priporočena diagnostična metoda, vendar je bila, zaradi premajhnih zmogljivosti na nacionalnem nivoju, rentgenska diagnostika z irigografijo še pogosto prva ali celo edina diagnostična preiskava. Pri raku danke je bila rigidna rektoskopija v tem obdobju prva preiskava (v letu 1995 pri 25% bolnikov z rakom danke v Sloveniji), včasih so jo kombinirali z irigografijo ali s kolonoskopijo pred operacijo (1).

Kot sem že omenil pri raku debelega črevesa, je bilo na vseh kirurških oddelkih v Sloveniji hospitaliziranih 90–95% bolnikov z rakom debelega črevesa in danke. Trend k zdravljenju bolnikov z rakom danke samo na večjih kirurških oddelkih je viden v zadnjem desetletju predvsem pri lokalizaciji raka in spodnjih dveh tretjinah danke (2).

Princip kirurškega zdravljenja raka danke je bil v 80. letih radikalna monoblok resekcija (nizka sprednja resekcija pri raku zgornje in srednje tretjine danke, abdominoperinealna ekscizija pri raku spodnje tretjine in večjih tumorjih srednje tretjine) z visoko ligaturo arterije mezenterike inferior (2). Avtomatski spenjalniki in dvojne staplerske anastomoze so postopoma zamenjale ročno šivanje anastomoz pri nizkih sprednjih resekcijah že v začetku 80. let in omogočile vse več radikalnih kontinentnih operacij. V 90. letih je postala kirurgija raka danke še radikalnejša. Seminarji ob začetku vseslovenske študije o raku debelega črevesa in danke, publikacija o raku danke ter dve kirurški delavnici in simpozija »Kirurgija širokega črevesa in danke« v 1996. letu in Zbornik »Kirurgija širokega črevesa in danke« so pripomogli k širjenju te kirurgije na druge kirurške oddelke (1, 3). Totalna mezorektalna ekscizija pa se je začela uvajati konec 90. let in še ni mogla imeti vpliva na tu prikazane rezultate.

Adjuvantno in paliativno onkološko zdravljenje se je na nacionalnem nivoju v opazovanem obdobju šele uveljavljalo. Bol-

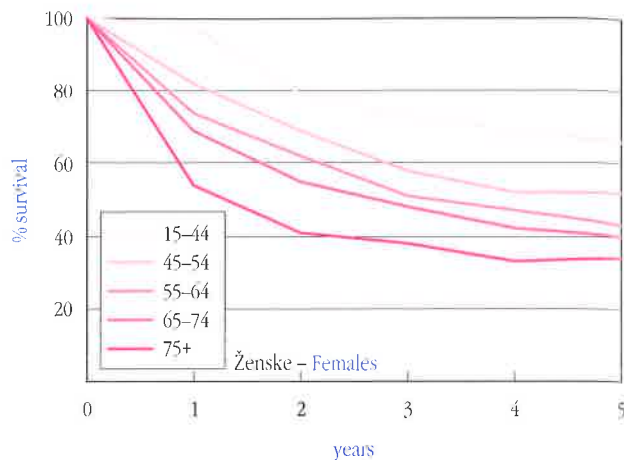


FIGURE 3: Relative five-year survival of rectal cancer patients diagnosed in the period 1993–1997 by age.

in male patients and in female patients 50.2% (49.1–51.4), while in Slovenia, it was 34% (30.3–38) in male patients and 35.2% (31.7–39.2) in female patients. The highest rates of 55.8% and of 63.4% were observed respectively in men in Switzerland (registries from Basel and Geneve only) and in women in three regions in France: Bas-Rhin, Calvados and Cote d'Or.

Stane Repše, Department of Abdominal Surgery, UMC, Ljubljana

In Slovenia, no screening for colorectal cancer has been so far introduced. Since the 1980s, the methods recommended in the diagnostics of rectal cancer have been colonoscopy and biopsy; however, due to the limited potentials of endoscopy at the national level, X-ray diagnostics with irrigography was often the method of choice or, in some cases, the only one. In those years, the first examination of a patient with rectal cancer was rectoscopy, performed by a rigid endoscope (e. g. in 1995, it was performed in as much as 25% of patients with colorectal cancer), occasionally, it was applied in combination with preoperative irrigography or colonoscopy (1).

As already mentioned in the chapter on the colon cancer, 90–95% of patients with colorectal cancer were hospitalized at the surgical units of the general hospitals of Slovenia. A trend to treat rectal cancer, particularly when it develops in the inferior two thirds of the rectum, only at the surgical departments of major hospitals was observed only in the last decade (2). In the 1980s, radical monoblock resection with a high ligation of the inferior mesenteric artery was considered as standard surgical treatment of rectal cancer (low anterior resection of the rectal tumor located at the superior and medium thirds of the rectum, abdominoperineal excision of the tumor located at the inferior third of the rectum and of larger tumors located at the medium third of the rectum) (2). In early 1980s, automatic stapler and double-stapler of anastomoses gradually replaced the classic manual sewing of anastomoses in inferior-anterior resections. In the 1990s, the surgery of the

niki so se praviloma zdravili na Onkološkem inštitutu. Neoadjuvantna radioterapija se je začela uvajati šele proti koncu 90. let.

Za 9% boljše relativno 5-letno preživetje bolnikov v obdobju 1993–97 na nacionalnem nivoju v primerjavi z obdobjem 1983–87, je posledica nekoliko hitrejše diagnostike, uvajanja sodobnih principov operacijskega zdravljenja na večini kirurških oddelkov, boljšega pooperacijskega in specifičnega onkološkega zdravljenja.

Zanimivo je, da je v tem obdobju za 5% padel delež lokalizirane bolezni na danki pri moških in pri ženskah in da se je dvignil delež bolnikov z regionalno, bolj napredovano boleznijo: pri moških za 6% in pri ženskah za 4%. Delež bolnikov z oddaljenimi zasevki je v tem obdobju pri moških padel za 1%, pri ženskah pa se je povišal za 2% (tabela 2). To kaže na boljše zamejevanje bolezni pred operacijo zaradi natančnejših preiskovalnih metod (ultrazvok, endoultrazvok, računalniška tomografija, MRI), med operacijo (intraoperativni ultrazvok) in na standardizirano definitivno patološko zamejitev bolezni na reseciranjem preparatu.

Prizadevanja zadnjih 15 let za multidisciplinarno obravnavo in multimodalno zdravljenje teh bolnikov, za lažjo dostopnost do endoskopskih preiskav, za preventivne preglede skupin z visokim tveganjem in endoskopsko odstranjevanje preneoplastičnih lezij, za standardizirano kirurško zdravljenje (na večjih kirurških oddelkih), specifično onkološko zdravljenje in redno sledenje reseciranih bolnikov bodo pokazala boljše rezultate zdravljenja na nacionalnem nivoju v naslednjem obdobju (3).

France Marolt, Onkološki inštitut Ljubljana

Že omenjena študija OIGIT (4) je doprinesla k sistematičnemu timskeemu pristopu primarnega zdravljenja lokalno napredovanih malignomov danke (T3–T4), kar je lahko prispevalo k 9% izboljšanju relativnega petletnega preživetja bolnikov. Dodatna radio- in kemoterapija se je programirala in izvajala po že izvršeni operaciji.

Po letu 1997 so se izpopolnili operativni pristopi, ob tem pa je prišlo tudi do spremembe pri načrtovanju primarnega zdravljenja. Neoadjuvantno obsevalno in cistostatsko zdravljenje se je pričelo uvajati pred operativnim posegom lokalno napredovanih tumorjev. Od tega in pa predvsem od zgodnejše diagnoze bolnikov si obetamo boljše rezultate v naslednjem petletnem obdobju.

Upamo, da bodo sodobne diagnostične metode in hitrejši diagnostični postopki v zadostni meri dostopni vsem bolnikom v Sloveniji. Le tako bomo lahko v večjem odstotku ugotavljali in zdravili bolnike z omejeno boleznijo.

Janja Ocvirk, Onkološki inštitut Ljubljana

Glede na rezultate raziskav v 90. letih je adjuvantna kemoterapija standarden način zdravljenja bolnikov s karcinomom debelega črevesa, stadija III (5). Zanimivo je, da rezultati raziskav, kjer so bili vključeni bolniki s karcinomi debelega čre-

rectum became more radical. The seminars organized at the start of a comprehensive Slovenian study, a publication, two workshops and symposia held in 1996 and the proceedings, all related to the »Surgery of the colon and rectum« had an influential role in promoting a more radical surgery of the colon and rectum at other surgical departments (1, 3). Total mesorectal excision (TME) was initiated at the end of the 1990s; therefore, it could not have any influence on the present data.

In comparison to the five-year survival rate at the national level in 1983–87, an increase of 9% was observed in the period 1993–97 that is attributable to a more rapid and precise diagnostics, to the introduction of most recent standards of surgical treatment at the majority of surgical departments in Slovenia, and to the improved postoperative and specific cancer treatments.

The application of adjuvant and palliative oncologic therapies came into use only in the last observation period. As a rule, the patients are referred to the Institute of Oncology for these therapies. Neoadjuvant radiotherapy was introduced in the late 1990s.

It is amazing that the percentage of locally advanced rectal cancer declined in males and females by 5%, and that it increased in regional and metastatic disease in males and females by 6% and 4%, respectively. The percentage of the patients with distant metastases decreased by 1% in males and increased by 2% in females (Table 2). This may prove that the disease staging has improved: the preoperative staging by the routine use of more precise examination methods (ultrasonography, endoscopic ultrasonography, computer tomography, magnetic resonance imaging), the intraoperative staging by intraoperative ultrasonography, as well as postoperative staging by the standardization of pathology staging of the disease on the resected sample.

The recent 15 years of best endeavors were aimed to enhance the multidisciplinary and multimodal approach to the treatment of patients, to facilitate the access to preventive endoscopic examination in high-risk groups of patients and as an endoscopic means for removing preneoplastic lesions, to standardize surgical treatment only at major surgical departments, to further develop specific cancer treatment and to follow-up the patients after resection. All these endeavors will give better treatment results at the national level not until the next observation period (3).

France Marolt, Institute of Oncology Ljubljana

OIGIT, the earlier mentioned study (4), has contributed substantially to a systematic and team approach to primary treatment of locally advanced cancer of the rectum (T3–T4), which also helped to increase the relative five-year survival by 9%. Adjuvant radiotherapy and chemotherapy were planned to be applied postoperatively.

Since 1997, after some advances have been made in surgical treatment, more changes have been introduced into the planning of primary treatment. In locally advanced disease, neoadjuvant radiotherapy and chemotherapy have been applied preoperatively. This change of treatment plan, togeth-

vesa in danke stadiju III, kažejo, da imajo dobrobit od adjuvantnega zdravljenja le bolniki s karcinomom debelega črevesa, ne pa tudi bolniki s karcinomom danke (6). Logično bi bilo sklepanje, da ima adjuvantna kemoterapija enak vpliv na karcinom danke kot na karcinom debelega črevesa, saj sta del istega organa. Eden izmed razlogov, zakaj pri bolnikih s karcinomom danke z dopolnilno kemoterapijo ne izboljšamo preživetja tako kot pri bolnikih s karcinomom debelega črevesa, je lahko dejstvo, da je večina raziskav vključila bolnike, ki so bili operirani po stari klasični kirurški metodi, ne pa po metodi TME kirurgije (totalne mezorektalne ekscizije). Dobrobit sistemskega zdravljenja se ni pokazala zaradi velikega števila lokalnih recidivov. V teku je več raziskav, ki proučujejo vpliv adjuvantne kemoterapije pri bolnikih s karcinomom danke po optimalni operaciji in obsevanju. Upamo, da nam bodo te raziskave dale več informacij o vrednosti adjuvantne kemoterapije pri bolnikih s karcinomom danke.

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er with earlier diagnosis of rectal cancer will hopefully have a favorable effect on the treatment outcome that can predict better results only in the next observation period.

We expect that the latest diagnostic methods and faster diagnostic procedures will be readily accessible to all patients in Slovenia. This is the only way that could enhance our chances to detect and also treat the disease in its locally advanced stage in a larger number of patients.

Janja Ocvirk, Institute of Oncology Ljubljana

With regard to the research results of the 1990s, the adjuvant chemotherapy seems to be the standard treatment of the patients with the colon cancer, stage III (5). It is interesting to note that the research results of the studies that included the patients with the stage III cancer of the colon and rectum indicate that the adjuvant treatment had a favorable effect only on the patients with colon cancer and none on the patients with rectal cancer (6). It should be reasonable that the adjuvant therapy had the same effect on the rectal cancer as well as on colon cancer, as they are both parts of the same organ. One of the reasons why the survival of the patients with rectal cancer is not improved as much as it is that of the patients with colon cancer may lie in the fact that most of the studies included the patients that had not been treated by TME but had undergone the classic surgical method. Systemic treatment was less effective because of numerous local recurrences that are resistant to systemic therapy. A number of studies are being carried out, dealing with the effect of adjuvant therapy on the patients with the rectal carcinoma following an optimal surgical intervention and irradiation. We expect that these studies will provide us with the more valuable data on the real usefulness of adjuvant chemotherapy of the patients with rectal carcinoma.

JETRA

LIVER

MKB 8 / ICD 8: 155

V obdobju 1983–97 je zbolelo za primarnim jetrnim rakom 498 moških in 268 žensk, od tega v letih 1993–97 222 moških in 123 žensk. V analizo ni bilo vključenih 167 (22%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca primarnega jetrnega raka večala. V letih 1983–87 je bila groba incidenčna stopnja 2,4/100.000 moških in 1,4/100.000 žensk, v letih 1993–97 pa 4,6/100.000 moških in 2,4/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je zmanjšal s 95% v letih 1983–87 na 89% v letih 1993–97. Med mikroskopsko potrjenimi tumorji je bilo v letih 1993–97 65% hepatocelularnih karcinomov, 26% holangiokarcinomov, 8% neopredeljenih karcinomov in žlezni karcinomov ter posamezni primeri hepatoblastoma, rabdoidnega in mešanoceličnega karcinoma.

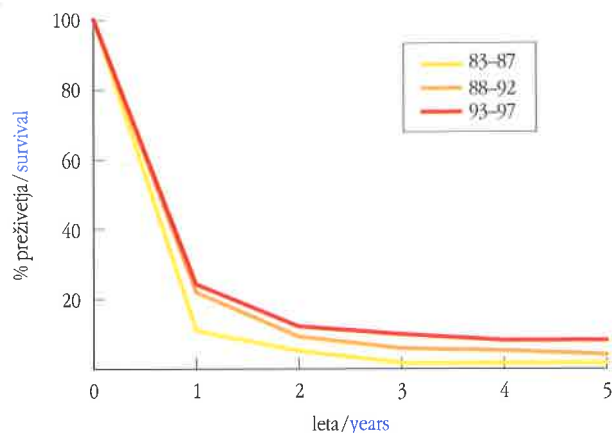
Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je zbolelo več bolnikov, mlajših od 55 let. Razširjenost bolezni ob diagnozi se je spremenila. V letih 1993–97 je bilo odkrite več bolezni v omejenem stadiju (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih samo 27% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (40%) samo kirurško, v 36,5% citostatsko, v 10% kirurško in citostatsko, v 6% samo obsevalno in v 3% obsevalno in citostatsko,

TABELA 1: Jetra. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Liver. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	71	1	2	7	32	20	9
Males	1988-92	129	3	8	14	49	38	17
	1993-97	180	1	13	29	62	57	18
Ženske	1983-87	51	1	4	4	9	23	10
Females	1988-92	66	2	2	8	19	17	18
	1993-97	102	1	9	11	12	52	17



SLIKA 1: Relativno petletno preživetje bolnikov z rakom jeter, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of liver cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 498 male and 268 female patients were diagnosed with primary liver cancer; of these, 222 males and 123 females were diagnosed with this cancer in the period 1993–97. In 167 patients (22%), liver cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of this cancer was increasing. In 1983–87, the crude incidence rate was 2.4/100,000 in males and 1.4/100,000 in females, whereas in 1993–97, it was 4.6/100,000 in males and 2.4/100,000 in females.

In comparison to 1983–87, a decrease of microscopically confirmed cases from 95% to 89% was observed in the period 1993–97. In the years 1993–97, the percentage of hepatocellular carcinomas, cholangiocarcinomas, and non-specified carcinomas together with adenocarcinomas in the microscopically confirmed primary liver cancer was 65%, 26%, and 8%, respectively; in addition, there were some individual cases of hepatoblastoma, rhabdoid-cell and mixed-cell carcinomas.

The age distribution of the patients included into the analysis has changed (Table 1). In the period 1993–97, the number of patients younger than 55 years was higher. The stage

TABELA 2: Jetra. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

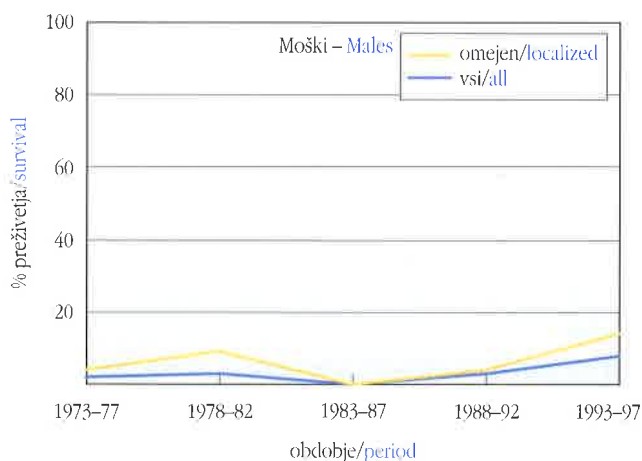
TABLE 2: Liver. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij / Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%			
Moški	1983-87	71	24	33,8	16	22,5	28	39,4	3	4,2
Males	1988-92	129	67	51,9	24	18,6	28	21,7	10	7,8
	1993-97	180	87	48,3	28	15,6	54	30,0	11	6,1
Ženske	1983-87	51	15	29,4	16	31,4	16	31,4	4	7,8
Females	1988-92	66	25	37,9	17	25,8	13	19,7	11	16,7
	1993-97	102	31	30,4	29	28,4	24	23,5	18	17,6

TABELA 3: Jetra. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Liver. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	4	(0-8)	0	(-)	0	(-)	19	(8-30)	4	(0-9)	2	(0-5)
1988-92	19	(12-26)	4	(1-7)	2	(0-4)	24	(14-34)	8	(1-15)	5	(1-9)
1993-97	24	(18-30)	10	(5-15)	7	(3-11)	22	(14-30)	8	(3-13)	6	(1-11)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	4	(0-8)	0	(-)	0	(-)	19	(8-30)	5	(0-10)	2	(0-6)
1988-92	20	(13-27)	4	(1-7)	3	(1-5)	25	(15-35)	8	(1-15)	5	(0-10)
1993-97	25	(19-31)	11	(6-16)	8	(3-13)	22	(14-30)	9	(3-15)	7	(2-12)



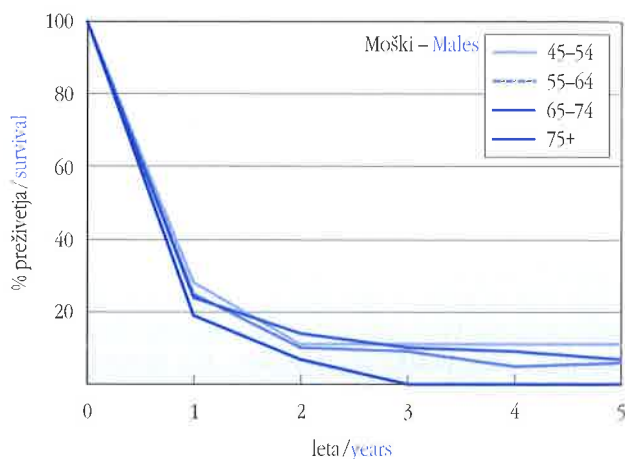
SLIKA 2: Relativno petletno preživetje bolnikov z rakom jeter, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

FIGURE 2: Relative five-year survival of liver cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

imunoterapijo so dodali v 2%, v 2% pa način zdravljenja Registru ni bil sporočen. V 45% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 32% na Kliničnem oddelku za abdominalno kirurgijo KC v Ljubljani, v 15% v SB v Mariboru, v 5% na Kliničnem oddelku za gastroenterologijo KC in v 2% na Pediatrični kliniki KC v Ljubljani.

V letih 1993-97 je bilo relativno petletno preživetje za 7% večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo pri bolnikih z omejeno boleznijo. Pri bolnikih, mlajših od 75 let, je bilo preživetje večje kot pri starejših (slika 3).

Primerjava podatkov o preživetju bolnikov med evropskimi državami ni možna zaradi različnega šifriranja primarnih tumorjev, jetrnih metastaz in neopredeljenih tumorjev.



SLIKA 3: Relativno petletno preživetje bolnikov z rakom jeter, zbolelih v letih 1993-1997 po starosti.

FIGURE 3: Relative five-year survival of liver cancer patients diagnosed in the period 1993-1997 by age.

distribution at diagnosis has changed, too. In the last observation period 1993-97, a higher percentage of patients with localized disease was observed (Table 2).

In the period 1993-97, 27% of patients underwent specific treatment. Surgery alone was applied as primary treatment in 40% of patients, 36.5% of patients received only chemotherapy as primary treatment, 10% underwent surgery and chemotherapy, 6% were treated with radiotherapy alone, 3% with radiotherapy and chemotherapy, and 2% of patients were additionally treated with immunotherapy, whereas the treatment modality applied in 2% of patients was not reported to the Registry. Primary treatment was started at the Institute of Oncology Ljubljana in 45% of patients, in 32% at the Department of Abdominal Surgery, UMC in Ljubljana, 15% in

Saša Markovič, Klinični oddelek za gastroenterologijo KC

povečanje incidenčne stopnje za primarne jetrnocelične karcinome (HCC) so v zadnjih letih opazili v vseh državah blagostanja. V bodočnosti lahko pričakujemo še nadaljnje povečanje. Prvi vzrok za to je velik odstotek okuženih s hepatitisom C. Drugi vzrok je daljše preživetje bolnikov z jetrno cirozo, ki je prekanceroza; HCC v 95% vznikne v cirotičnih jetrih. Tretji vzrok pa je, da je v obdobju od leta 1993 začela potekati med gastroenterologi usmerjena akcija zgodnjega odkrivanja HCC pri bolnikih z jetrno cirozo, ki jo je sprožilo Slovensko združenje za gastroenterologijo in hepatologijo. Vse bolnike z jetrno cirozo smo spremljali na pol leta z merjenjem koncentracije alfafetoproteina v serumu in ultrazvočnim pregledom jeter. Tumorje smo tako odkrili prej in starost novoo odkritih bolnikov se je znižala. Istočasno je pričela v svetu veljati mednarodno sprejeta doktrina, da je pri bolniku z jetrno cirozo z ultrazvočno vidno fokalno lezijo in alfafetoproteinom >400 dovolj dokazov, da gre za HCC in da histološke in citološke potrditve niso potrebne.

Pri bolnikih s HCC je kriterij za zdravljenje odvisen od stopnje jetrne ciroze – zaradi katere tudi večina bolnikov umre. Smrt pri HCC ni povezana s tumorjem, pač pa z napredovano stopnjo jetrne ciroze. Napredovana stopnja kot je označena po Childu s stopnjo C onemogoča zdravljenje jetrnih tumorjev. S tem si lahko razložimo tudi majhen odstotek specifično zdravljenih bolnikov v Sloveniji.

V letu 1993 smo pričeli prek Slovenskega združenja za gastroenterologijo in hepatologijo izdelovati nacionalne smernice diagnostike in zdravljenja. Zdravljenje je potekalo po nacionalnem dogovoru in protokolu, kar se je odrazilo na bolj primernem izboru bolnikov za zdravljenje. Za zdravljenje smo se odločali glede na velikost tumorja in stopnjo jetrne bolezni. Na novo je bilo uvedeno določanje zamejitve jetrne bolezni po Child-Pughu in zamejitve jetrnih tumorjev po Okudi. Kirurško zdravljenje je bilo opravljeno le pri zgodnjih tumorjih in pri bolnikih z zadovoljivo jetrno funkcijo. V začetnem obdobju smo pri nekaterih tumorjih kombinirali metodo preoperativne kemoembolizacije za zmanjšanje tumorja in potem prešli na operacijo, vendar smo zaradi slabih rezultatov to kmalu prekinili. Visok odstotek samo operiranih (40%) pomeni, da je bilo presejanje uspešno. Citostatsko zdravljenje, ki smo ga uporabljali, je bila kemoembolizacija z mešanico lipiodola in mitomycina C. Uporabili pa smo ga samo pri bolnikih z zadovoljivo jetrno funkcijo in pri tistih, ki zaradi multifokalnega vznika tumorja niso bili primerni za operacijo. Kasneje smo začeli s perkutano alkoholno sklerozacijo, katere izid je podoben izidu jetrne kirurgije, in s tem še nadaljujemo. Danes zaradi uvedbe transplantacije jeter presejanje bolnikov z jetrno cirozo izvajamo še bolj striktno, ker je transplantacija edino ozdravitveno zdravljenje za majhne HCC. Obsevalno zdravljenje pri HCC ni na mestu in tudi ni učinkovito, indicirano je samo za poskus paliacije pri velikem povečanju jeter in s tem povezanih težavah.

Na Onkološkem inštitutu je leta 1993 pričel delovati redni multidisciplinarni konzilij za jetrne tumorje. Tam so bili predstavljeni skoraj vsi bolniki iz Slovenije. V letih 1993–97 je potekala

the General Hospital in Maribor, in 5% at the Department of Gastroenterology, UMC in Ljubljana and 2% at the Department of Paediatric Surgery and Intensive Care, UMC in Ljubljana.

The relative five-year survival rate was 7% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The survival improved in the patients with localized diseases and was higher in the patients aged less than 75 years than in the patients older than that (Figure 3).

The comparison of the survival rate of liver cancer patients in Slovenia with the survival rates in other European countries is not possible because these countries apply different coding for primary tumors, liver metastases and non-specified tumors.

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In the recent years, an increase in the incidence rate of primary hepatocellular carcinoma (HCC) has been observed in the countries of general wealth and prosperity. In the years to come, we may expect that it will continue to rise. The main reason is a very high proportion of population contracted with hepatitis C. The second reason is an improved survival of the patients with the cirrhosis of the liver, which is known to be precancerous; actually, 95% of HCC develop from the cirrhotic liver. The third reason is that the Slovenian gastroenterologists gathered in the joint program for early detection of HCC in the patients with the cirrhosis of the liver that was initiated by the Slovenian Association of Gastroenterology and Hepatology. All patients with the cirrhosis of the liver had the alpha-fetoprotein concentration in the serum measured and an US examination of the liver made every six months at the follow-up controls. That way, the tumors were detected earlier, whereas the age of the patients with newly detected liver cancer declined accordingly. At the same time, new guidelines were adopted worldwide advocating that if the patient with liver cirrhosis has a focal lesion detected by ultrasound and alpha-fetoprotein concentration >400, there is enough evidence that he developed HCC; therefore, further histology and cytology confirmations are not necessary.

The standard of treating the patients with HCC depends upon the stage of liver cirrhosis, which is a true cause of death in the majority of these patients. The patients with HCC die from liver cirrhosis in the advanced stage rather than from HCC. The stage C, termed according to Child, is the advanced stage that does not allow going ahead with treating HCC. This may also explain why the percentage of patients who received specific therapy is so small in Slovenia.

In 1993, we started to draw up national guidelines for diagnostics and treatment of HCC in cooperation with the Slovenian Association of Gastroenterology and Hepatology. We followed National Agreement and Protocol, which resulted in a more convenient selection of the patients eligible for treatment. The treatment plans were made with regard to the tumor size and stage of the liver cirrhosis. In disease staging, we used the most recently introduced Child-Pugh's and Okuda's staging methods for liver diseases and liver tumors, respectively. Surgery

na Onkološkem inštitutu in sočasno v Trstu tudi prospektivna študija (1). Na Kliničnem oddelku za abdominalno kirurgijo KC in v SB Maribor so potekale zahtevne jetrne operacije.

VIR

1. Markovič S, Gadžijev E, Štabuc B et al. Treatment options in Western hepatocellular carcinoma: a prospective study of 224 patients. *J Hepatol* 1998; 29: 650–9.

was performed only in the patients with tumors in early stages and with satisfactory renal function. At first, we combined pre-operative chemoembolisation in order to reduce the size of tumor and surgery; but the results were so poor that we gave up that treatment modality. A considerably high percentage (40%) of the patients operated on indicates that screening was successful. The therapy with cytostatics that we applied comprised chemoembolization using a combination of lipiodol and mitomycin C. This therapy was given only to the patients with satisfactory renal function and those who were not eligible for surgery because of multifocal tumor growth. Later on, a percutaneous ethanol injection was applied. This treatment modality has a similar outcome as surgery; we therefore keep on using it. With the initiation of liver transplantation, the screening for liver cirrhosis has become even more strict, because the small-size HCC are curable only with the transplantation of the liver. Radiotherapy of HCC is not recommendable and not effective either. It is indicated only as palliative treatment of pain due to the excessively enlarged liver.

Since 1993, a Multidisciplinary Advisory Team for Hepatic Tumors has been regularly held at the Institute of Oncology. So far, almost all Slovenian patients with hepatic carcinoma were presented at this team. In the years 1993–1997, a prospective study (1) was being performed simultaneously at the Institute of Oncology in Ljubljana and in Trieste. At the departments of abdominal surgery of UMC Ljubljana and of General Hospital Maribor, numerous difficult and most demanding operations on the liver were carried out.

SEČNI MEHUR

BLADDER

MKB 8 / ICD 8: 188

V obdobju 1983–97 je zbolelo za invazijskim rakom sečnega mehurja 1873 moških in 643 žensk, od tega v letih 1993–97 706 moških in 268 žensk. V analizo ni bilo vključenih 111 (4%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti. V analizo tudi niso bili vključeni bolniki s karcinomom in situ, ki jih Register redno spremlja šele od leta 1995. Le-ti bi povečali število bolnikov, vključenih v analizo za 25% in bi tako zanesljivo vplivali na dobljene izsledke o preživetju.

V opazovanem 15-letnem obdobju se je incidenca invazijskega raka sečnega mehurja večala. V letih 1983–87 je bila groba incidenčna stopnja 12,4/100.000 moških in 3,5/100.000 žensk, v letih 1993–97 pa 14,7/100.000 moških in 5,2/100.000 žensk.

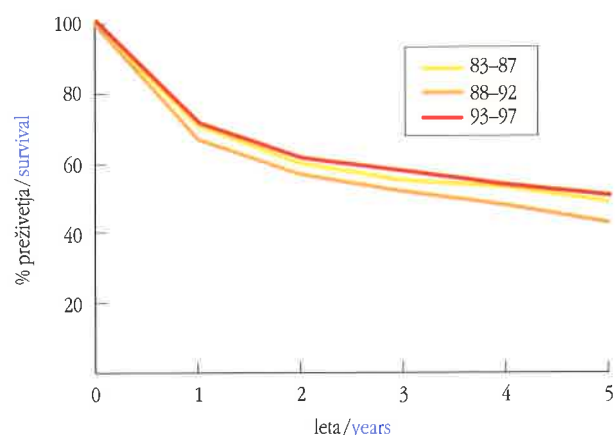
Odstotek mikroskopsko potrjenih primerov se je povečal s 94% v letih 1983–87 na 95% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 91% prehodnoličnih karcinomov, 2% žlezni karcinomov in 2% ploščatoceličnih karcinomov. Neopredeljenih in drugih malignih tumorjev je bilo 5%.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila, v letih 1993–97 je bilo zajetih več starejših bolnikov (tabela 1). Razširjenost bolezni ob diagnozi je bila v letih 1988–1992 manj ugodna kot v letih 1983–87 in 1993–1997 (tabela 2).

TABELA 1: Sečni mehur. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Bladder. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87	564	0	16	52	134	177	185
	1988-92	564	0	9	54	141	170	190
	1993-97	682	0	20	50	163	280	169
Ženske Females	1983-87	166	0	4	8	33	50	71
	1988-92	185	0	5	7	45	51	77
	1993-97	244	1	4	17	36	93	93



SLIKA 1: Relativno petletno preživetje bolnikov z rakom sečnega mehurja, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of bladder cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 1,873 male and 643 female patients were diagnosed with invasive cancer of the bladder; of these, 706 males and 268 females were diagnosed with this cancer in the period 1993–97. In 111 patients (4%), bladder cancer was diagnosed at death; these patients were therefore not included in the analysis, neither were the patients with in-situ carcinoma who have been regularly followed by the Registry since 1995. Were they included into the analysis, the number of patients would rise by 25%. This would certainly have an effect upon the obtained survival rates.

In the observed 15-year period, the incidence of this cancer was increasing. In the period 1983–87, the crude incidence rate was 12.4/100,000 in males and 3.5/100,000 in females, whereas in 1993–97, it was 14.7/100,000 in males and 5.2/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 1%, i. e. from 94% to 95%. In the years 1993–97, the percentage of transitional-cell carcinomas, adenocarcinomas, and squamous-cell carcinomas in the microscopically confirmed cases of the bladder cancer was 91%, 2%, and 2%, respectively; in addition, 5% were non-specified and other malignant tumors.

The age distribution of patients included into the analysis has changed. In the period 1993–97, the number of elderly

TABELA 2: Sečni mehur. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

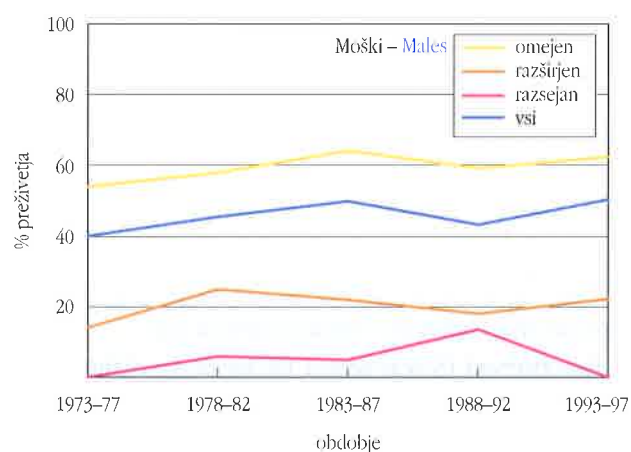
TABLE 2: Bladder. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznani/ Unknown	%				
Moški Males	1983-87	564	347	61,5	119	21,1	27	4,8	71	12,6
	1988-92	564	302	53,5	156	27,7	28	5,0	78	13,8
	1993-97	682	442	64,8	150	22,0	30	4,4	60	8,8
Ženske Females	1983-87	166	88	53,0	47	28,3	2	1,2	29	17,5
	1988-92	185	76	41,1	59	31,9	11	5,9	39	21,1
	1993-97	244	153	62,7	56	23,0	15	6,1	20	8,2

TABELA 3: Sečni mehur. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Bladder. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	68	(64-72)	46	(42-50)	36	(32-40)	63	(55-71)	43	(35-51)	35	(28-42)
1988-92	66	(62-70)	46	(42-50)	32	(28-36)	56	(49-63)	37	(30-42)	33	(26-40)
1993-97	68	(64-72)	49	(45-53)	37	(33-41)	66	(60-72)	45	(39-51)	38	(32-44)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	72	(68-76)	56	(51-61)	50	(44-56)	66	(58-74)	50	(41-59)	46	(36-56)
1988-92	70	(66-74)	55	(50-60)	43	(38-48)	59	(52-66)	43	(35-51)	43	(34-52)
1993-97	72	(68-76)	58	(53-63)	50	(45-55)	70	(64-76)	54	(46-62)	50	(42-58)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom sečnega mehurja, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

V letih 1993-97 je bilo specifično zdravljenih 93% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (67%) samo kirurško, kombinirano: operacija, obsevanje, kemoterapija v 13%, operacija in obsevanje v 9%, operacija in kemoterapija v 8%, operacija in imunoterapija v 2%. Pri večini operiranih bolnikov je bila narejena samo transuretralna resekcija (TUR). Registru raka so za obdobje 1993-97 javili le 77 totalnih cistektomij (13% operiranih). Deleži posameznih načinov zdravljenja so bili v letih 1988-92 enaki, v letih 1983-87 pa je bil delež samo operiranih bolnikov ter operiranih in obsevanih pomembno večji; delež tistih, ki so prejeli kemoterapijo, pa manjši. V 47% so pričeli s prvim zdravljenjem na Kliničnem oddelku za urologijo KC v Ljubljani, v 10% v SB Šempeter pri Novi Gorici, po 9% v SB v Mariboru in v Celju, v 8% v SB v Novem mestu, v 6% v SB v Slovenj Gradcu, v 4% v SB v Izoli, v 3% v SB v Murski Soboti in v 2% v SB na Jesenicah. Na Onkološkem inštitutu v Ljubljani so pričeli prvo zdravljenje pri 3% bolnikov.

V letih 1993-97 je bilo relativno petletno preživetje samo za 1% večje kot v letih 1983-87 (slika 1). Preživetje se pri posameznih

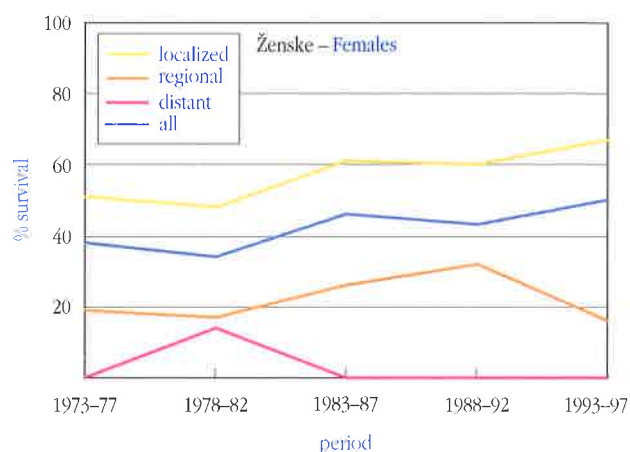
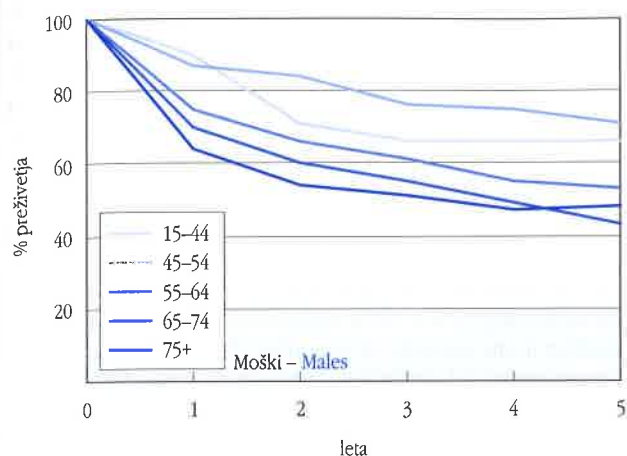


FIGURE 2: Relative five-year survival of bladder cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

patients was higher (Table 1). The stage distribution at diagnosis was less favorable in the observation period 1988-92 than in 1983-87 and 1993-97 (Table 2).

In the period 1993-97, 93% of patients underwent specific treatment. Surgery alone was applied as primary treatment in the highest percentage of patients (67%), 13% of patients received combined treatment of surgery, radiotherapy and chemotherapy, 9% were treated with surgery and radiotherapy, 8% underwent surgery and chemotherapy, and 2% surgery and immunotherapy. In the majority of patients, transurethral resection (TUR) was performed. The Registry received reports of only 77 total cystectomies (13% of all operated patients) made in the period 1993-97. The percentages of individual treatment modalities were the same also in the years 1988-1992, whereas in the years 1983-87, the percentages of the patients who underwent surgery alone and of those who were treated surgically and irradiated were significantly higher, while of those who received chemotherapy alone, it was lower. Primary treatment was started at the Department of Urology, UMC in Ljubljana in 47% of patients, in 10% in the General



SLIKA 3: Relativno petletno preživetje bolnikov z rakom sečnega mehurja, zbolelih v letih 1993–1997 po starosti.

stadijih bolezní ni povečalo (slika 2). Preživetje je bilo pri moških, starih 55–64 let za 14% manjše kot pri mlajših (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka sečnega mehurja pri moških 70,9% (70–71,8) in pri ženskah 68,5% (67,1–70), v Sloveniji pa pri moških 45,2% (40,1–50,9) in pri ženskah 56,4% (49,3–64,6). Največje preživetje pri moških je bilo 84,9% na Islandiji in pri ženskah 77,4% na Tirolskem v Avstriji. Primerjava med državami pa ni verodostojna, ker je Slovenija v analizo vključila samo bolnike z invazivskim rakom.

Boris Sedmak, Klinični oddelek za urologijo KC

Zgodnja diagnoza raka mehurja je ključnega pomena za boljšo prognozo. Na vseh uroloških oddelkih v Sloveniji sta se kot najpomembnejši preiskavi za diagnozo raka sečnega mehurja uporabljali cistoskopija in histopatološka ocena tkiva po endoskopski resekciji. Razširjenost bolezní je bila ocenjevana predvsem z ultrazvočno preiskavo, računalniško tomografijo, magnetno resonanco, intravenozno urografijo in bimanuelno palpacijo v anesteziji med TUR tumorja mehurja. Citološka analiza urina je bila uporabljena večinoma za sledenje uspešnosti zdravljenja in manj pri začetni diagnostiki. Pri zamejevanju bolezní je bila uporabljena TNM klasifikacija.

Površinski raki sečnega mehurja Ta-T1 so bili zdravljeni s TUR in v primeru ponovitve poleg TUR še z intravezikalnimi instilacijami BCG ali mitomycina. Karcinom in situ je bil poleg TUR zdravljen še z instilacijami BCG.

Invazivni raki sečnega mehurja bi morali biti v opazovanem obdobju v večji meri zdravljeni z radikalno cistektomijo. Radikalna cistektomija je zlati standard zdravljenja mišično-invazivskih tumorjev prehodnoceličnega epitela mehurja v večini držav po svetu. Indikacije zanjo so mišično-invazivni karcinom mehurja T2-T4a, N0-NX, M0 in obsežni površinski papilarni rak mehurja, ki ga ni mogoče zdraviti s konzervativnimi metodami. Poleg inkontinentnih derivacij so bile

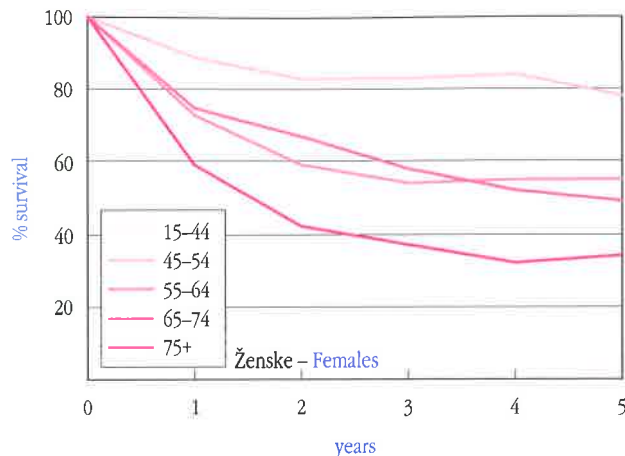


FIGURE 3: Relative five-year survival of bladder cancer patients diagnosed in the period 1993–1997 by age.

Hospital Šempeter pri Novi Gorici, in 9% in each of General Hospitals in Maribor and in Celje, in 8% in the General Hospital in Novo mesto, in 6% in the General Hospital in Slovenj Gradec, in 4% in the General Hospital in Izola, in 3% in the General Hospital in Murska Sobota, and in 2% in the General Hospital in Jesenice. At the Institute of Oncology, the primary treatment was started only in 3% of patients.

The relative five-year survival rate was only 1% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The survival at each individual stage of the disease did not improve (Figure 2). The survival of male patients in the age group of 55–64 years was 14% lower than that of younger male patients (Figure 3).

According to the EURO CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with bladder cancer was 70.9% (70–71.8) in male patients and in female patients 68.5% (67.1–70), while in Slovenia, it was 45.2% (40.1–50.9) in male patients and 56.4 (49.3–64.6) in female patients. The highest rates of 84.9% and of 77.4% were observed respectively in male patients in Iceland and in female patients in Tyrol in Austria. The comparison between countries may not be reliable because, in Slovenia, only the patients with invasive bladder cancer were included into the study.

Boris Sedmak, Department of Urology, UMC, Ljubljana

Early diagnosis of bladder cancer is of essential importance for a more favorable prognosis. In the urology departments of the general hospitals in Slovenia, the diagnostics of bladder cancer is based on two fundamental examination methods, i. e. cystoscopy and histopathology of the tissue samples collected by endoscopic resection. The disease stage evaluation is made by ultrasonography, computer tomography, magnetic resonance imaging, intravenous urography and bimanual palpation during TUR of the bladder tumor with the patient under anaesthesia. Cytology of the urine is mainly used

predvsem pri mlajših bolnikih narejene tudi kontinentne-Cock pouch ali ortotopni mehur iz segmentov tankega in debelega črevesa.

V izbranih primerih je bilo uporabljeno kratkotrajno preoperativno obsevanje in adjuvantna kemoterapija. V primeru, da je bolnik odklanjal cistektomijo in v izbranih primerih je bil bolnik zdravljen s kombiniranim zdravljenjem – TUR, kemoterapijo in obsevanjem. V primeru neobčutljivosti tumorja na kemo- in radioterapijo ali pri ponovitvi tumorja po predhodnem obsevanju in kemoterapiji je bila narejena cistektomija. Rezultati kombiniranega načina zdravljenja so bili pri teh skrbno izbranih bolnikih dobri (1). Pogoji za kombinirano zdravljenje je dobro sodelovanje med urologi in onkologi. V Ljubljani imamo sodelavci Kliničnega oddelka za urologijo KC in Onkološkega inštituta skupne urološko-onkološke konzilije, na katerih obravnavamo bolnike z rakom sečnega mehurja, ki so se zdravili pri nas v Ljubljani, in bolnike, ki so bili poslani na konzilij iz drugih uroloških oddelkov v Sloveniji.

Tanja Čufer, Onkološki inštitut Ljubljana

5-letno preživetje bolnikov z rakom sečnega mehurja se v opazovanem 15-letnem obdobju v Sloveniji ni spremenilo. V obdobju 1988–92 smo bili celo priča nekoliko slabšemu preživetju, verjetno na račun manjšega deleža omejene bolezni. V zadnjem obdobju pa smo spet na ravni iz let 1983–87. To preseneča, kajti operativne tehnike kirurškega zdravljenja, ki je še vedno temeljni način zdravljenja tega raka, so se izpopolnile (2). Dodatno so se izboljšale tudi obsevalne tehnike, dobili smo učinkovite citostatike za prehodnoceličnega raka (2). Razlog, da se preživetje od sedemdesetih let ni izboljšalo, je iskati v premalo izkoriščenih možnostih multidisciplinarnega zdravljenja (3) in v nezadostni kirurgiji. Podatki za zadnje obdobje 1993–97 kažejo, da je bilo samo okoli 30% bolnikov deležnih poleg kirurškega zdravljenja še obsevanja ali kemoterapije. Samo 13% bolnikov je bilo zdravljenih s kombinacijo vseh treh načinov zdravljenja. Večina, 67% bolnikov je bilo zdravljenih samo s kirurgijo. Pri večini operiranih je bila narejena samo TUR, kar ni zadostno zdravljenje za invazijskega raka sečnega mehurja (2). V obdobju 1993–97 je bilo Registru prijavljenih samo 77 totalnih cistektomij (13%). Majhen delež ustreznih zdravljenih bolnikov za invazijskega raka sečnega mehurja: z radikalno cistektomijo ali pa s kombinacijo TUR, kemoterapijo in obsevanjem (4) je razlog slabemu preživetju. Porazdelitve zdravljenj po posameznih opazovanih obdobjih ne kažejo premikov k ustrežnejšemu zdravljenju in temu primerno ostaja preživetje enako slabo.

Večje preživetje bolnikov z razsejano boleznijo v obdobju 1988–92 je posledica uvedbe učinkovitih citostatikov v zdravljenje prehodnoceličnega raka (5, 6). To pa smo izkoristili le pri razsejani in ne pri manj napredovani bolezni.

Za 14% manjše preživetje pri bolnikih, starejših od 55 let glede na mlajše, ni pričakovano. Glede na izpopolnjene kirurške in anestezijske metode bi se razlike v učinkovitosti zdravljenja glede na starost bolnikov morale manjšati in ne večati (1). Manjše preživetje je lahko posledica neustreznega izpeljanega zdravljenja ali odtegnitve zdravljenja starejšim bolnikom.

in the follow-up of the patients in order to assess the effectiveness of treatment, while in initial diagnostics, its use is less frequent. The disease is staged according to TNM classification.

Superficial bladder tumors, stages Ta-T1, were treated by TUR and, in case of recurrence, by TUR and by intravesical instillation of BCG vaccine or mitomycin. In *in situ* carcinomas (Tis), the instillation of BCG vaccine was applied in addition to TUR.

In the observed period, the invasive bladder cancers should have been treated to a larger extent by radical cystectomy. Radical cystectomy is the gold standard in the treatment of muscle-infiltrating tumors of the transitional-cell epithelium of the bladder in the majority of countries. The indications for this surgery are muscle-infiltrating carcinomas of the bladder, stage T2-T4a, N0NX, M0, and advanced epithelial papillary-cell carcinomas of the bladder that cannot be treated by conservative methods. In younger men, in addition to incontinent derivations, continent-Cock pouch bladders or orthotopic bladders were constructed from the sections of the small intestine and the colon.

In a few selected cases, short-term preoperative radiotherapy and adjuvant chemotherapy were applied. The patients who refused cystectomy and a few selected patients were treated by TUR of the bladder followed by chemotherapy and radiotherapy. If tumors were not responsive to chemotherapy and radiotherapy and in case of their recurrence after preoperative chemotherapy or radiotherapy, cystectomy was performed. The results of this combined treatment modality in these selected patients were good (1). Combined treatment modality may be successful only on condition that there is a mutual and close cooperation between the urologist and oncologist. The medical staff of the Department of Urology, UMC, Ljubljana, and the medical staff of the Institute of Oncology Ljubljana meet regularly at the meetings of the Multidisciplinary Advisory Team for Urinary Bladder Tumors and discuss the cases of the patients who have been treated in Ljubljana and of those who have been referred to our team from the departments of urology at other hospitals in Slovenia.

Tanja Čufer, Institute of Oncology Ljubljana

The five-year survival of the patients with bladder cancer did not change in the 15-year observation period. It was even worse in the period 1988–92, which was most probably due to a decreased percentage of the patients with localized disease. In the most recent observation period, it reached the same level as in the 1983–87 period. This, in fact, is rather surprising because, in surgery, which remains the basic primary treatment of this cancer, a number of techniques were considerably improved (2). At the same time, the irradiation techniques were improved, too, and in addition to all that, new, most effective cytostatics started to be applied in the treatment of transitional-cell carcinomas (2). The reason for practically no improvement of the survival since the 1970s lies in neglecting the potentials of multidisciplinarity in cancer treatment (3) and in inadequate surgery. The data of the last observation period 1993–97 indicate that only 30% of surgically treated patients received postoperative radiotherapy or chemotherapy. Only 13% of patients were treated with the combination

Podatki kažejo na premajhno uporabo radikalne cistektomije in multidisciplinarnega pristopa k zdravljenju raka sečnega mehurja v Sloveniji. Preživetje bi lahko izboljšali s primernejšo izbiro in izvedbo tako kirurškega kot dodatnega obsevalnega in citostatskega zdravljenja pri vseh bolnikih in z boljšo oskrbo starejših bolnikov.

VIRI

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of all three treatment modalities and the majority of them (67%) underwent surgery alone. In the majority of surgically treated patients, only TUR was performed, which is certainly not a sufficiently radical surgical intervention in the treatment of invasive bladder cancer (2). In the 1993–97 period, only 77 total cystectomies (13%) were reported to the Registry. A low percentage of the invasive bladder cancer patients who have received proper treatment, *viz.* radical cystectomy or TUR in combination with chemotherapy and radiotherapy, is another factor that contributes to the poor survival of these patients (4). The distribution of treatment modalities in each observation period does not show any favorable shifts to a more proper treatment; therefore, no such shifts can be expected in the survival which remains poor accordingly.

An improved survival of the patients with advanced disease in the period 1988–92 is the result of the application of the then new and effective cytostatic drugs in the treatment of transitional-cell carcinoma of the bladder (5, 6). Hence, only the patients with advanced disease benefited from the use of these drugs and none of those with less advanced disease.

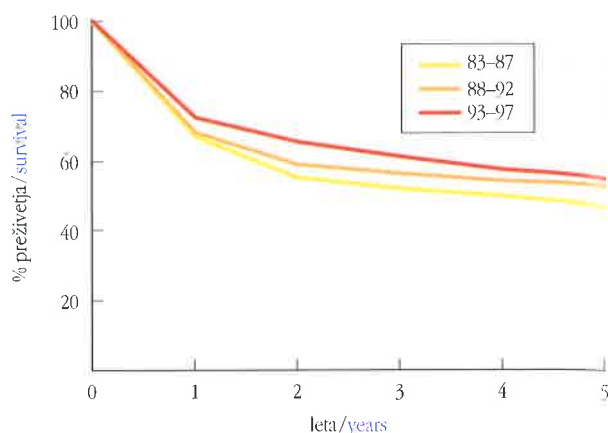
A comparison of the survivals of older and younger patients showed a drop of 14% in the survival of patients older than 55 years, which was not expected. Considering the improvements made in surgery techniques and in anesthesia, the differences in the treatment effectiveness with regard to the age of the patients should start to fall down instead of growing up (1). A poorer survival probably results from an inadequate treatment planning and its carrying out or from withdrawal of elderly patients from treatment.

The data indicate that, in Slovenia, radical cystectomy and multidisciplinary approach are severely underestimated in the treatment of the bladder cancer patients. The survival could be essentially improved by a more appropriate planning and carrying out of surgery and of adjuvant radiotherapy and chemotherapy in all bladder cancer patients and by a more careful care of elderly patients.

LEDVICA

KIDNEY

MKB 8/ICD 8: 1890



SLIKA 1: Relativno petletno preživetje bolnikov z rakom ledvic, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of renal cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za ledvičnim rakom (brez ledvičnega meha) 1134 moških in 787 žensk, od tega v letih 1993–97 503 moški in 354 žensk. V analizo ni bilo vključenih 157 (8%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca ledvičnega raka večala. V letih 1983–87 je bila groba incidenčna stopnja 6,1/100.000 moških in 3,5/100.000 žensk, v letih 1993–97 pa 10,6/100.000 moških in 7,1/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov je bil ves čas opazovanja 89%. Med mikroskopsko potrjenimi tumorji je bilo v letih 1993–97 95% žlezni karcinomov, 2% neopredeljenih in slabo diferenciranih karcinomov ter 3% kompleksnih mešanih in stromalnih malignomov (nefroblastomi, adenosarkomi, karcinosarkomi).

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila, v zadnjih letih 1993–97 je bilo zajetih več bolnikov v starosti 65–74 let (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila. Pri obeh spolih se je zmanjšal delež neznanega stadija. Pri moških se je povečal delež omejene bolezni, pri ženskah pa razširjene in razsejane bolezni (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 85% bolnikov. Pri odraslih je bilo prvo zdravljenje v največjem odstotku (85%) samo kirurško, v 2% kirurško in obsevalno in v 2% samo

In the period 1983–97, a total of 1,134 male and 787 female patients were diagnosed with renal cancer (excluding the renal pelvis); of these, 503 males and 354 females were diagnosed with this cancer in the period 1993–97. In 157 patients (8%), renal cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of renal cancer was increasing. In the period 1983–87, the crude incidence rate was 6.1/100,000 in males and 3.5/100,000 in females, whereas in 1993–97, it was 10.6/100,000 in males and 7.1/100,000 in females.

The percentage of microscopically confirmed cases (89%) was the same throughout the whole observation period. In the years 1993–97, the percentage of adenocarcinomas, and of non-differentiated- and poorly differentiated-cell carcinomas in the microscopically confirmed cases of the renal cancer was 95% and 2%, respectively; in addition, 3% were complex mixed and stromal neoplasms (nephroblastomas, adenosarcomas, carcinosarcomas).

The age distribution of patients included into the analysis has been changing. In the period 1993–97, a higher number of patients aged from 65 to 74 years were included in the analysis (Table 1). The stage distribution at diagnosis changed. In

TABELA 1: Ledvica. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Kidney. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	255	7	23	44	86	66	29
Males	1988-92	312	5	26	59	87	87	48
	1993-97	472	9	46	74	139	150	54
Ženske	1983-87	153	8	12	26	42	41	24
Females	1988-92	236	2	21	34	75	63	41
	1993-97	336	10	20	40	93	128	45

TABELA 2: Ledvica. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

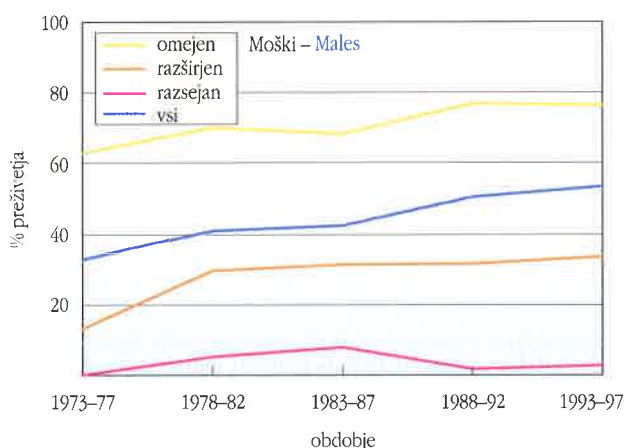
TABLE 2: Kidney. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Omejen/ Localized	Stadij / Stage			Neznan/ Unknown	%		
				Razširjen/ Regional	Razsejan/ Distant	%				
Moški	1983-87	255	116	45,5	41	16,1	77	30,2	21	8,2
Males	1988-92	312	168	53,8	49	15,7	70	22,4	25	8,0
	1993-97	472	283	60,0	73	15,5	92	19,5	24	5,1
Ženske	1983-87	153	92	60,1	20	13,1	23	15,0	18	11,8
Females	1988-92	236	138	58,5	30	12,7	46	19,5	22	9,3
	1993-97	336	195	58,0	51	15,2	61	18,2	29	8,6

TABELA 3: Ledvica. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Kidney. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	60	(54-66)	42	(36-48)	35	(29-41)	72	(65-79)	55	(47-63)	49	(41-57)
1988-92	64	(59-69)	48	(42-54)	41	(35-47)	86	(81-91)	72	(65-79)	65	(58-72)
1993-97	70	(66-74)	55	(50-60)	44	(39-49)	70	(65-75)	58	(53-63)	50	(44-56)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	63	(57-69)	47	(40-54)	42	(35-49)	74	(67-81)	59	(50-68)	56	(47-65)
1988-92	67	(61-73)	54	(48-60)	50	(43-57)	69	(63-75)	59	(52-66)	55	(48-62)
1993-97	73	(69-77)	61	(56-66)	53	(47-59)	72	(67-77)	62	(56-68)	56	(50-62)



SLIKA 2: Relativno petletno preživetje bolnikov z rakom ledvic, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.

obsevalno. Kombinirano zdravljenje (ob operaciji in/ali obsevanju še kemoterapija in/ali imunoterapija) je bilo uporabljeno v 6%. Pri 5% bolnikov je bila narejena samo embolizacija tumorja. Bolniki so v 49% pričeli s prvim zdravljenjem na Kliničnem oddelku za urologijo KC v Ljubljani, v 12% v SB v Mariboru, v 7% v SB v Celju, v 6% v SB v Slovenj Gradcu, po 5% v SB v Novi Gorici in Novem mestu, v 3% v SB v Murski Soboti, v 2% na Pediatrični kliniki, po 1% v SB v Izoli in na Jesenicah ter na Kliničnem oddelku za abdominalno kirurgijo KC. Na Onkološkem inštitutu v Ljubljani je pričelo prvo zdravljenje 6% bolnikov, posamezni bolniki so pričeli s prvim zdravljenjem še na Interni kliniki in Kliničnem oddelku za nevrokirurgijo ter v SB Brežice in Ptuj.

V letih 1993–97 je bilo relativno petletno preživetje za 8% večje kot v letih 1983–87 (slika 1). Preživetje se je dejansko povečalo samo pri moških (tabela 3). Preživetje se je povečalo pri moških z omejeno in razširjeno boleznijo, pri ženskah pa samo pri omejeni bolezni (slika 2). Preživetje je bilo največje pri bolnikih starih 45–54 let (slika 3).

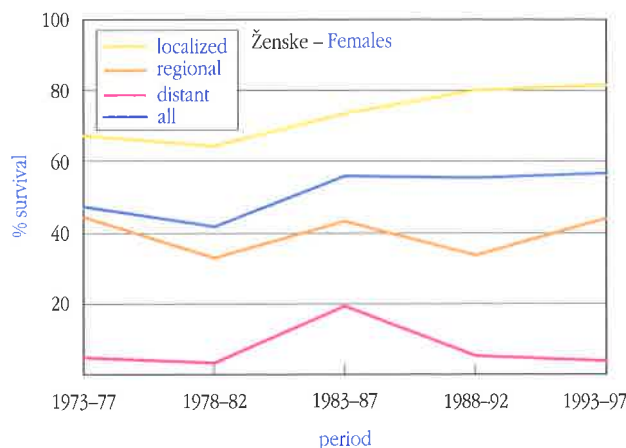
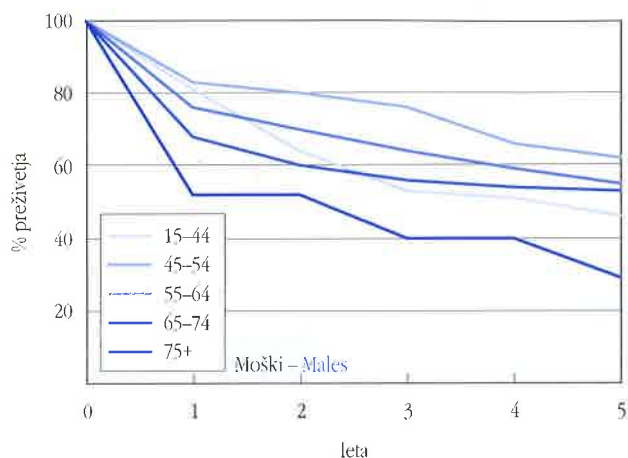


FIGURE 2: Relative five-year survival of renal cancer patients diagnosed in the period 1973–1997 by stage and period of diagnosis.

both sexes, the percentage of the disease of unknown stage decreased. In male patients, an increase of localized disease was observed, whereas in female patients, of regional and metastatic disease (Table 2).

In the period 1993–97, 85% of patients underwent specific treatment. Surgery alone was applied as primary treatment in the highest percentage of adult patients (85%), 2% of patients received combined treatment of surgery and radiotherapy, 2% were treated with radiotherapy alone, 6% underwent concomitant treatment of surgery and/or radiotherapy with chemotherapy and/or immunotherapy. Embolization of tumor was performed in 5% of patients. Primary treatment was started at the Department of Urology, UMC in Ljubljana in 49% of patients, in 12% in the General Hospital in Maribor, in 7% in the General Hospital of Celje, in 6% in the General Hospital in Slovenj Gradec, in 5% in each of General Hospitals in Šempeter pri Novi Gorici and in Novo mesto, in 3% in the General Hospital Murska Sobota, in 2% at the Department of Paediatrics, UMC, Ljubljana, in 1% in each of the General Hospitals in Izola and Jesenice and at the Department for



SLIKA 3: Relativno petletno preživetje bolnikov z rakom ledvic, zbolelih v letih 1993–1997 po starosti.

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka ledvic pri moških 53,1% (51,4–54,8) in pri ženskah 55,6% (53,9–57,4), v Sloveniji pa pri moških 43,5% (37,3–50,6) in pri ženskah 47,9% (41,4–55,3). Največje preživetje pri moških in pri ženskah je bilo na Tirolskem v Avstriji: 66,2% oziroma 67,1%.

Mirjana Žumer - Pregelj, Klinični oddelek za urologijo KC

Zgodnje odkrivanje se je izboljšalo samo pri moških zaradi večje uporabe ultrazvočnih preiskav; podoben pojav smo opazili za ženske že v 80. letih. Zgodnje odkrivanje je izredno pomembno, saj je relativno petletno preživetje pri omejeni bolezni 81% pri ženskah oziroma 77% pri moških. Z zgodnejšim odkrivanjem bolezni si lahko razložimo tudi dejstvo, da je preživetje pri obeh spolih v starosti 45–54 let najboljše. Pri mlajših od 45 let je bil delež omejene bolezni za 11% manjši kot v starosti 45–54 let. Pri njih se še ne pomisli na raka in je zato odkrivanje bolezni zakasnelo. Pri starejših bolnikih, starih 65–74 let pa je bil delež zgodaj odkritih za 16% manjši. Ali smo v letih 1993–97 pri njih v manjši meri uporabljali ultrazvočne preiskave in nismo v zadostni meri upoštevali rizičnih skupin?

Izboljšanje petletnega preživetja za 8% gre izključno na račun izboljšanja preživetja pri moških za 11%, kar potrjuje dejstvo, da je stadij bolezni najpomembnejši napovedni dejavnik preživetja.

Način zdravljenja se v tem obdobju ni pomembno spremenil. Večina odraslih bolnikov je bila samo operiranih (v letih 1993–97 za 7% več kot v letih 1983–87). Operativno zdravljenje je še vedno edino učinkovito zdravljenje. Samo embolizacija tumorja (5%) je bila narejena pri bolnikih z močno napredovanim tumorjem, ki je lokalno neoperabilen, pri bolnikih z razsejano boleznijo in bolnikih, ki niso primerni za operacijo. Pri manjšem odstotku je bila embolizacija del kombiniranega primarnega zdravljenja (embolizacija in nato operacija).

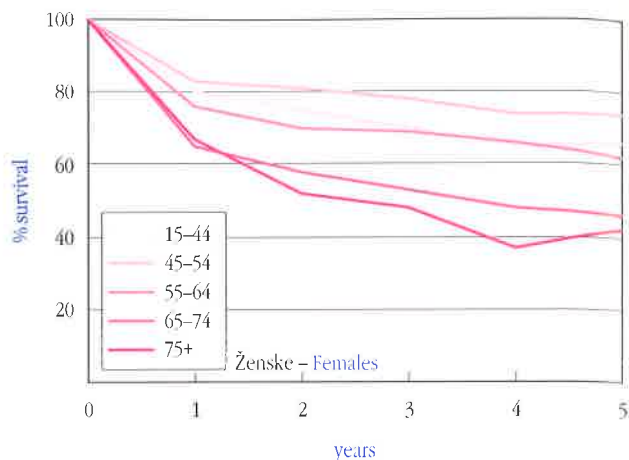


FIGURE 3: Relative five-year survival of kidney cancer patients diagnosed in the period 1993–1997 by age.

Abdominal Surgery, UMC in Ljubljana. At the Institute of Oncology in Ljubljana, primary treatment was started in 69% of patients and a few individual patients received primary treatment at the Department of Internal Medicine and at the Department of Neurosurgery, both of UMC in Ljubljana and in the General Hospitals in Brežice and Ptuj.

The relative five-year survival rate was 8% higher in the years 1993–97 than in the years 1983–87 (Figure 1). Actually, the survival improved only in male patients (Table 3). Better survival was observed in male patients with localized and regional disease and in female patients with localized disease (Figure 2). The highest improvement in survival was noted in the patients in the age group of 45–54 years (Figure 3).

According to the EURO CARE-3 study results for the period 1990–94, in Europe, the age-standardized relative survival rate of the patients with renal cancer was 53.1% (51.4–54.8) in male patients and in female patients 55.6% (53.9–57.4), while in Slovenia, it was 43.5% (37.3–50.6) in male patients and 47.9% (41.4–55.3) in female patients. The highest rates of 66.2% and of 67.1% were observed respectively in male and female patients in Tyrol in Austria.

Mirjana Žumer - Pregelj, Department of Urology, UMC, Ljubljana

Early detection of renal cancer has improved only in men on the account of more extensive use of ultrasonography (US). A similar trend was observed in female patients in the 1980s. Early detection is of paramount importance considering the fact that the relative five-year survival of female and male patients with localized disease is 81% and 77%, respectively. The early detection of the disease may account for the most improved survival of the patients of both sexes in the age group of 45–54 years. In the patients younger than that, the localized disease percentage was 11% lower than in those in the age group of 45–54 years. In these patients, a suspect of renal cancer hardly ever arises; therefore, the detection of the dis-

Vzrok za podpovprečno mesto Slovenije v skupini EURO CARE je premajhen odstotek omejene bolezni, zlasti pri mlajših in starejših bolnikih. Z občasnimi ultrazvočnimi pregledi rizičnih skupin po 65. letu starosti bi lahko ugotovili večje število bolnikov z omejeno boleznijo in s tem povečali preživetje.

Borut Kragelj, Onkološki inštitut Ljubljana

Možnost ozdravitve raka ledvic je odvisna od obsega bolezni, verjetnost ozdravitve je ob regionalnih zasevkih kot tudi pri preraščanju tumorja v sosednje organe manj kot 20%. Že ob diagnozi pa lahko pričakujemo (tabela 2) v 25–30% oddaljene zasevke.

Osnovno zdravljenje omejene bolezni je kirurško, delna ali popolna nefrektomija z odstranitvijo venskega trombusa in ob preraščanju ledvice tudi kar se da radikalno odstranitvijo izven ledvice ležečega tumorja z ali brez odstranitve regionalnih bezgavk. Dopolnilno obsevanje kot tudi sistemsko zdravljenje, tudi če je omejeno na visoko rizično skupino bolnikov z regionalnimi zasevki in vraščanjem tumorja v sosednje organe, ne vpliva na možnost ozdravitve. Osnova sistemskega zdravljenja je imunoterapija, ki vključuje interleukin 2 in interferon α ali β . Slednja je občasno kombinirana s citostatiki (vinblastin, ciklofosfamid) ali dodatnimi imunomodulatorji (1).

Na preživetje bolnikov z rakom ledvic lahko vplivamo le s pravočasno diagnozo in kakovostno kirurško oskrbo. Na žalost pa je velik del bolnikov skoraj v celoti asimptomatskih (hematurija je prisotna le pri približno 40% bolnikov) ali pa se tumor kaže z nenavadnimi znaki, ki so povezani s paraneoplastičnim sindromom. Klasičen trias ledvena oteklina in bolečina ter hematurija je prisoten pri manj kot 10% bolnikov in še to tedaj ko je bolezen že razsejana.

VIR

1. Marston Linehan W, Zbar B, Bates SE, Zelefsky MJ, Yang JC. Cancer of the kidney and urether. In: deVita VTJr, Hellman S, Rosenberg SA, eds. Cancer: principles and practice of oncology. 6th ed. Philadelphia: Lippincott, 2001: 1362–95.

ease is rather delayed. In older patients, aged between 65 and 74 years, the percentage of early-detected cases is lower by 16%. Is it possible that US examinations were performed less frequently in the years 1993–97 and that the risk groups were not adequately taken into account?

The 8 percent rise of five-year survival is attributable exclusively to the improved survival in men, which increased by 11%. This may well be the proof that the disease stage is one of the most important prognostic factors.

The treatment modality did not change significantly in this period. The majority of elderly patients underwent surgery alone (in the period 1993–97, the percentage of only surgically treated patients was 7% higher than in the period 1983–87). Surgery is still considered to be the only effective treatment. Tumor embolization alone (5%) was performed in the patients with extremely advanced and locally inoperable tumor, in those with distant metastases, and in those who were not eligible for surgery. In very low percentage of patients, the embolization was performed as a part of combined treatment and was followed by surgery.

The reason why Slovenia ranks so low in the EURO CARE group is a too low percentage of localized disease in younger as well as in elderly patients. Should we start with periodic examinations of the risk population aged over 65 years, we would probably detect more patients with localized disease and thus contribute immensely to an increase in the survival.

Borut Kragelj, Institute of Oncology Ljubljana

The prospects of cure for renal cancer depend on the stage of disease and are very low, less than 20%, for the patients with the disease at regional stage and for those with tumor infiltrating into neighboring organs. Distant metastases may too often, in 25–30% of cases, be detected already at diagnosis.

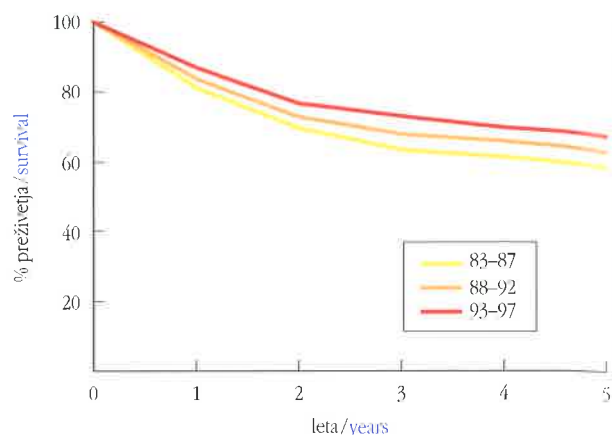
Surgery is undoubtedly the basic primary treatment of this cancer. Usually, partial or total nephrectomy is performed removing also the vein thrombus. In case of locally advanced tumor, radical removal of the tumor with or without lymph node dissection is performed. Neither adjuvant radiotherapy nor systemic treatment, though restricted to a high risk group of patients with regional metastases and tumor infiltration into neighboring organs, have any significant effect on the prospect of cure. The systemic treatment is primarily based on immunotherapy applying interleukin-2 and interferon α and β . Immunotherapy is often combined with chemotherapy applying vinblastine and cyclophosphamide or additional immunomodulators (1).

The survival of patients with renal cancer can be improved only by early diagnosis and high quality surgical treatment. Unfortunately, the majority of renal cancer patients are asymptomatic (hematuria is observed in about 40%) or the tumor has the symptoms related to a paraneoplastic syndrome. A classic triad comprising flank edema, pain and hematuria is detected in less than 10% of patients and most often only when the cancer has already developed distant metastases.

MATERNIČNI VRAT

CERVIX UTERI

MKB 8 / ICD 8: 180



SLIKA 1: Relativno petletno preživetje bolnic z rakom materničnega vratu, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of cervical cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom materničnega vratu 2677 bolnic, od tega v letih 1993–97 1006. V analizo ni bilo vključenih 14 (0,5%) bolnic, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju je bila incidenca raka materničnega vratu sprva ustaljena, sredi 90. let pa se je povečala. V letih 1983–87 je bila groba incidenčna stopnja 16,9/100.000 žensk, v letih 1993–97 pa 19,7/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal z 99% v letih 1983–87 na 100% v letih 1993–97. Med mikroskopsko potrjenimi je bilo 78% ploščatoceličnih, 17% žleznih in 4% neopredeljenih karcinomov.

Starostna porazdelitev v analizo zajetih bolnic se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnic mlajših od 55 let. Razširjenost bolezni ob diagnozi se je spremenila. V letih 1993–97 je bilo več bolezni v omejenem stadiju (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 97% bolnic. Prvo zdravljenje je bilo v 39% samo kirurško, v 33% samo obsevalno (tele in/ali brahiradioterapija), v 25% kirurško in obsevalno. Citostatsko zdravljenje samo ali v kombinaciji z operacijo ali obsevanjem je bilo uporabljeno v 3%. Prvo zdravljenje se je pričelo v 48% na Onkološkem inštitutu v Ljubljani, v 31% na Ginekološki kliniki v Ljubljani, po 4% v SB v Celju in Mariboru, po 2% v SB v Izoli, Slovenj Gradcu in v Kranju, po 1% v SB v Novem mestu in na Ptujju ter v bolnišnici v Postojni, po 0,5% v SB v Brežicah in v Murski Soboti. Manjše število bolnic je bilo zdravljenih v zasebnih ordinacijah in v SB na Jesenicah.

TABELA 1: Maternični vrat. Bolnice vključene v analizo po starosti in obdobju opazovanja.

TABLE 1: Cervix uteri. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi/ Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Ženske Females	1983-87	824	0	265	140	203	132	84
	1988-92	839	0	350	126	172	113	78
	1993-97	1000	0	451	197	154	125	73

In the period 1983–97, a total of 2,677 female patients were diagnosed with cervical cancer; of these, 1,006 females were diagnosed with this cancer in the period 1993–97. In 14 patients (0.5%), cervical cancer was diagnosed at death; these patients were therefore not included in the analysis.

At the beginning of the observed 15-year period, the incidence of cervical cancer was rather stable, but in the mid 1990s, it increased. In the period 1983–87, the crude incidence rate was 16.9/100,000 females, whereas in 1993–97, it was 19.7/100,000 females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 1%, i. e. from 99% to 100%. In the years 1993–97, the percentage of squamous-cell carcinomas, adenocarcinomas, and non-specified carcinomas in the microscopically confirmed cases was 78%, 17% and 4%, respectively.

The age distribution of patients included into the analysis has been changing (Table 1). In the period 1993–97, a higher number of patients younger than 55 years were included in the analysis. The stage distribution at diagnosis also changed. In the period 1993–97, the percentage of localized disease was higher than that in two earlier periods (Table 2).

In the period 1993–97, 97% of patients underwent specific treatment. Surgery alone was applied as primary treatment in 39% of patients, 33% were only irradiated (tele- and/or brachyradiotherapy), 25% of patients received combined treatment of

TABELA 2: Maternični vrat. Bolnice vključene v analizo po stadiju bolezni in obdobju opazovanja.

TABLE 2: Cervix uteri. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij/Stage					Neznan/ Unknown	%		
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	%					
Ženske Females	1983-87	824	325	39,4	442	53,6	49	5,9	8	1,0
	1988-92	839	375	45,0	406	48,4	50	6,0	8	0,6
	1993-97	1000	529	52,9	422	42,2	43	4,3	6	0,6

TABELA 3: Maternični vrat. Opazovano in relativno petletno preživetje po obdobju opazovanja s 95 % intervalom zaupanja (IZ).**TABLE 3: Cervix uteri. Observed and relative five-year survival by period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano / Observed (%)					
	1		3		5	
	IZ/CI	Ženske / Females Leta / Years	IZ/CI	Ženske / Females Leta / Years	IZ/CI	Ženske / Females Leta / Years
1983-87	80	(77-83)	60	(57-63)	54	(50-58)
1988-92	83	(80-86)	65	(62-68)	59	(56-62)
1993-97	86	(84-88)	71	(68-74)	64	(61-67)

Obdobje/ Period	Relativno / Relative (%)					
	1		3		5	
	IZ/CI	Ženske / Females Leta / Years	IZ/CI	Ženske / Females Leta / Years	IZ/CI	Ženske / Females Leta / Years
1983-87	81	(78-84)	63	(59-67)	59	(55-63)
1988-92	84	(81-87)	68	(65-71)	63	(59-67)
1993-97	87	(85-89)	73	(70-76)	68	(65-71)

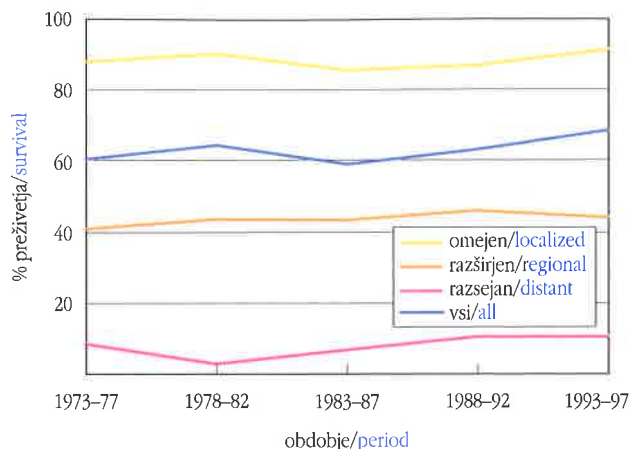
V letih 1993-97 je bilo relativno petletno preživetje za 9% večje kot v letih 1983-87 (slika 1). V primerjavi s preživetjem v 70. letih pa se v 90. letih preživetje ni pomembno povečalo (slika 2). Pri bolnicah, mlajših od 45 let, je bilo za 46% večje kot pri starih 75 let in več (slika 3).

Izsledki študije EUROCARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka materničnega vratu 59,9% (58,7-61,1), v Sloveniji 56,2% (52,5-60,1). Največje preživetje je bilo 66,8% v Švici (samo območji registrov Basla in Ženeve).

Peter Fras, Onkološki inštitut Ljubljana

Specifično onkološko zdravljenje raka materničnega vratu je kirurško, z obsevanjem, s kombinacijo obojega, v zadnjih letih pa še s kombinacijo s kemoterapijo. Samo kirurško zdravljenje se v zadnjih letih ni spremenilo. Pri bolnicah (39%), ki so bile zdravljene samo s kirurškim posegom, je bil rak diagnosticiran v začetnem, operabilnem stadiju bolezni. 25% bolnic je bilo obsevanih po predhodnem kirurškem posegu zaradi neugodnih napovednih dejavnikov. V določenem odstotku je možno kirurško zdravljenje tudi po predhodnem radikalnem obsevanju, če ni popolnega regresa ali se pojavi zgodnji recidiv («salvage surgery»). Kombinacija obsevanja in kemoterapije pri napredovanih stadijih raka materničnega vratu naj bi zagotavljala boljše rezultate zdravljenja. Zaradi premajhnega števila zdravljenih s tem načinom v Sloveniji svojih rezultatov še ne moremo oceniti.

Spoznanje, da je najuspešnejše zdravljenje določenih vrst raka v večjih centrih, upoštevamo, saj je večina bolnic z rakom materničnega vratu zdravljenih na Onkološkem inštitutu, Ginekološki kliniki v Ljubljani ter Ginekološkem oddelku Splošne bolnišnice v Mariboru. Še vedno pa se 17% zbolelih začne zdraviti v drugih ustanovah. V večini primerov gre za ome-

**SLIKA 2: Relativno petletno preživetje bolnic z rakom materničnega vratu, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.****FIGURE 2: Relative five-year survival of cervical cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.**

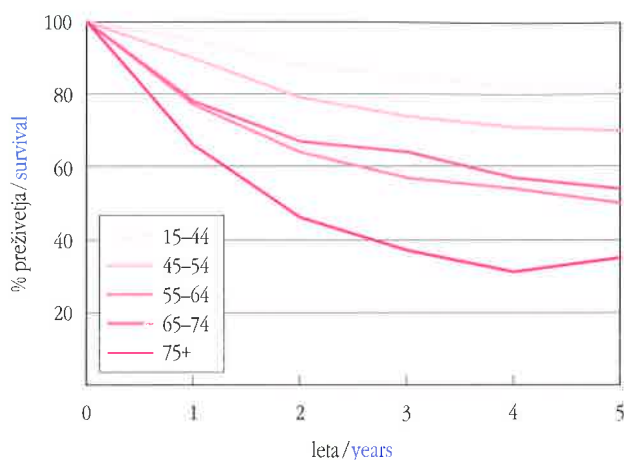
surgery and radiotherapy, 3% received chemotherapy alone or in combination with surgery and radiotherapy. Primary treatment was started at the Institute of Oncology in Ljubljana in 48% of patients, in 31% of patients, it was started at the Department of Obstetrics and Gynaecology, UMC in Ljubljana, in 4% in each of General Hospitals in Maribor and in Celje, in 2% in each of General Hospitals of Izola, Slovenj Gradec, and Kranj, in 1% in each of General Hospitals in Novo mesto, Celje, Ptuj and Postojna, and in 0.5% in each of General Hospitals in Brežice and in Murska Sobota.

The relative five-year survival rate was 9% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The survival in the 1990s, compared to that of the 1970s, did not significantly change in any of the disease stages (Figure 2). The survival of the patients younger than 45 years was by 46% higher than that of the patients over 75 years old (Figure 3).

According to the EUROCARE-3 study results for the period 1990-94, in Europe, the age-standardized relative survival rate of the patients with cervical cancer was 59.9% (58.7-61.1), while in Slovenia, it was 56.2% (52.5-60.1). The highest rate of 66.8% was recorded in Switzerland (only registries in Basel and Geneva).

Peter Fras, Institute of Oncology Ljubljana

Specific treatment of cervical cancer involves surgery and irradiation, a combination of both, and in recent years, also combined treatment with chemotherapy. In surgical treatment, no changes have been made lately. In 39% of patients who were treated by surgery alone, the cancer was diagnosed in its initial stage when it was still operable; 25% of patients received postoperative irradiation because of most unfavorable prognostic factors. In a certain percentage of patients, surgery can be carried out after radical radiotherapy if remission is not complete or if recurrence is detected. This is the so-called 'salvage



SLIKA 3: Relativno petletno preživetje bolnic z rakom materničnega vratu, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of cervical cancer patients diagnosed in the period 1993–1997 by age.

jeni IA stadij, včasih je bolezen ugotovljena naključno pri bolnicah, ki so se zdravile zaradi drugih ginekoloških obolenj.

Za 9% izboljšano relativno petletno preživetje v letih 1993–97 v primerjavi z leti 1983–87 kaže na izpopolnjene kirurške tehnike z ustrežno pooperativno nego, saj poleg tega, da zdravimo kirurško pretežno mlajše bolnice z lokalizirano boleznijo, zdravimo kirurško tudi starejše bolnice. Bistvenega izboljšanja petletnega preživetja v 90. letih v primerjavi s preživetjem v 70. letih ni bilo, kar potrjuje, da pri zdravljenju raka materničnega vratu ni bilo radikalnejših sprememb v načinu zdravljenja. Kombinacija vseh treh načinov zdravljenja, kirurškega, z obsevanjem in s kemoterapijo bo pokazala morebitno izboljšanje šele čez nekaj let.

VIRA

1. Fras P, ed. Doktrina zdravljenja ginekoloških malignomov. Ljubljana: Onkološki inštitut, 1992.
2. Stržinar V, Baškovič M, Behar S et al. Ginekološki malignomi: doktrina zdravljenja ginekoloških malignomov na Onkološkem inštitutu in Univerzitetni ginekološki kliniki. 2. rev. izd. Ljubljana: Zveza slovenskih društev za boj proti raku, 2001.

surgery'. A combination of irradiation and chemotherapy for the treatment of cervical cancer in the advanced stages is considered to yield better treatment results. Due to a limited number of patients who have been treated so far by this modality in Slovenia, we have not been able to make an evaluation of the treatment results.

We strictly hold on to the general rule saying that the treatment of certain cancer types is more effective and successful in larger medical centers. The majority of cervical cancer patients were treated at the Institute of Oncology Ljubljana, at the Department of Obstetrics and Gynaecology, UMC in Ljubljana and at the Department of Gynecology of the General Hospital in Maribor. Still, 17% of patients start their treatment in other institutions. These are usually the patients with the IA stage of the disease. In some cases, the disease was accidentally detected in the patients who were treated for other gynecological diseases

A 9 percent better relative five-year survival in the period 1993–97 than that in the period 1983–87 is the result of the improved surgical techniques and of a proper postoperative care of patients. As a matter of fact, we are treating surgically as much younger patients with localized disease as older ones. No significant improvement was observed in the five-year survival of the 1990s in comparison to that of the 1970s. This may be a proof that in the treatment modality of cervical cancer no radical changes were made. The effect of a combination of all three treatments, of surgery, radiotherapy and chemotherapy, on the eventual improvement of survival, will be seen only after a few years.

MATERNIČNO TELO

CORPUS UTERI

MKB 8 / ICD 8: 1820

V obdobju 1983–97 je zbolelo za rakom materničnega telesa 3015 bolnic, od tega v letih 1993–97 1228. V analizo ni bilo vključenih 31 (1%) bolnic, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka materničnega telesa večala. V letih 1983–87 je bila groba incidenčna stopnja 17,3/100.000 žensk, v letih 1993–97 pa 24/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov je bil ves čas opazovanja 99%. Med mikroskopsko potrjenimi je bilo v letih 1993–97 74% žleznih, 21% adenoskvamoznih, 2% neopredeljenih karcinomov in 3% kompleksnih mešanih in stromalnih malignomov.

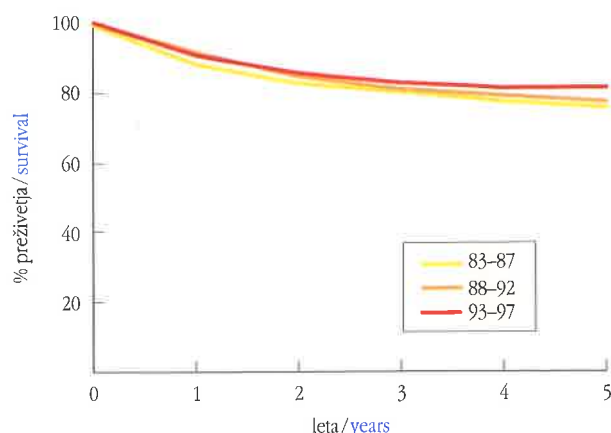
Starostna porazdelitev v analizo zajetih bolnic se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnic v starostni skupini od 65–74 let. Razširjenost bolezni ob diagnozi se ni pomembno spremenila (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 96% bolnic. Prvo zdravljenje je bilo v 60% kirurško in obsevalno (tele- in/ali brahiradioterapija), v 24% samo kirurško, v 12% samo obsevalno, v 2% v kombinaciji s kemoterapijo, v 3% v kombinaciji s hormonsko terapijo. Prvo zdravljenje se je pričelo v 42% na Ginekološki kliniki v Ljubljani, v 25% na Onkološkem inštitutu v Ljubljani, v 10% v SB v Mariboru, v 7% v SB v Celju, po 3% v SB v Šempetru pri Novi Gorici in Slovenj Gradcu, po 2% v SB v Izoli in Postojni, po 1% v SB v Kranju, v Novem

TABELA 1: Maternično telo. Bolnice vključene v analizo po starosti in obdobju opazovanja.

TABLE 1: Corpus uteri. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Ženske Females	1983-87	839	0	18	152	326	212	131
	1988-92	929	0	25	170	335	264	135
	1993-97	1216	0	42	191	396	389	198



SLIKA 1: Relativno petletno preživetje bolnic z rakom materničnega telesa, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of corpus uteri cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 3,015 female patients were diagnosed with the cancer of the corpus uteri; of these, 1,228 females were diagnosed with this cancer in the period 1993–97. In 31 patients (1%), corpus uteri cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of the cancer of the corpus uteri was increasing. In the period 1983–87, the crude incidence rate was 17.3/100,000 females, whereas in 1993–97, it was 24/100,000 females.

Throughout the observation period 1993–97, the percentage of microscopically confirmed cases was consistent, reaching 99%. In the years 1993–97, the percentage of adenocarcinomas, adenosquamous-cell carcinomas, non-specified carcinomas and complex mixed-type cell carcinomas together with stromal and complex mixed malignant tumors in the microscopically confirmed cases was 74%, 21%, 2%, and 3%, respectively.

The age distribution of patients included into the analysis has been changing (Table 1). In the period 1993–97, a higher number of patients of the age group of 65–74 years were included in the analysis. The stage distribution at diagnosis did not significantly change (Table 2).

In the period 1993–97, 96% of patients underwent specific treatment. Surgery in combination with irradiation (tele- and/or brachyradiotherapy) was applied as primary treatment in 60% of patients, 24% underwent surgery alone, 12% were only irra-

TABELA 2: Maternično telo. Bolnice vključene v analizo po stadiju bolezni in obdobju opazovanja.

TABLE 2: Corpus uteri. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%				
Ženske Females	1983-87	839	651	77,6	115	13,7	66	7,9	7	0,8
	1988-92	929	718	77,3	119	12,8	83	8,9	9	1,0
	1993-97	1216	924	76,0	185	15,2	80	6,6	27	2,2

TABELA 3: Maternično telo. Opazovano in relativno petletno preživetje po obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Corpus uteri. Observed and relative five-year survival by period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano / Observed (%)					
	Ženske / Females					
	Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	86	(84-88)	75	(72-78)	67	(64-70)
1988-92	90	(88-92)	76	(73-79)	68	(65-71)
1993-97	89	(87-91)	77	(75-79)	71	(68-74)

Obdobje/ Period	Relativno / Relative (%)					
	Ženske / Females					
	Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	89	(87-91)	81	(78-84)	76	(72-80)
1988-92	92	(90-94)	81	(78-84)	77	(74-80)
1993-97	91	(89-93)	83	(80-86)	81	(78-84)

mestu, na Jesenicah, na Ptuj in v Trbovljah ter po 0,5% v SB v Brežicah in Murski Soboti.

V letih 1993-97 je bilo relativno petletno preživetje za 5% večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo v vseh stadijih bolezni (slika 2). Pri bolnicah, mlajših od 65 let, je bilo za 19% oziroma 33% večje kot pri starejših (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka materničnega telesa 73,4% (72,2-74,6), v Sloveniji 72,8% (68,4-77,5). Največje preživetje je bilo 81,1% na Tirolskem v Avstriji.

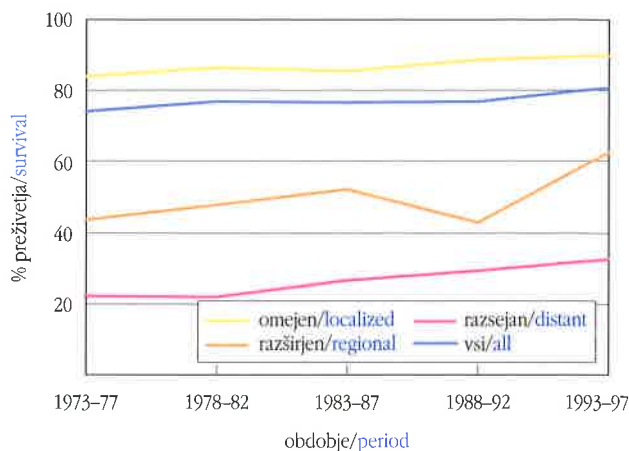
Peter Fras, Onkološki inštitut Ljubljana

Večanje incidence raka materničnega telesa ni vplivalo na število mikroskopsko potrjenih primerov, saj je še vedno 99%. Ta podatek potrjuje koristnost izdelane doktrine, saj ta predpisuje diagnostični postopek pri sumu na raka materničnega telesa. Večanje incidence pri ženskah, starejših od 75 let kaže na aktivnejši diagnostični postopek in izboljšanje predoperativnih priprav.

Povečano petletno preživetje bolnic z regionalno razširjeno boleznijo v obdobju 1993-97 v primerjavi z obdobjem 1983-87 pa prav tako kaže na upoštevanje doktrinarnih zahtev o nadaljevanju zdravljenja po kirurškem posegu.

Na Ginekološki kliniki v Ljubljani, na Onkološkem inštitutu ter Ginekološko-porodniškem oddelku Splošne bolnišnice v Mariboru se začne zdraviti 77% bolnic. Na ostalih ginekoloških oddelkih se jih začne zdraviti 23%. Specifično onkološko zdravljenje ni bilo mogoče pri 4% bolnic zaradi starosti, napredovane bolezni in spremljajočih drugih bolezni.

5% večje petletno preživetje v letih 1993-97 v primerjavi z leti 1983-87 kaže z veliko verjetnostjo na zgodnejše odkrivanje in tudi prosvetljenost žensk, da se že ob prvi pomeno-

**SLIKA 2: Relativno petletno preživetje bolnic z rakom materničnega telesa, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.****FIGURE 2: Relative five-year survival of corpus uteri cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.**

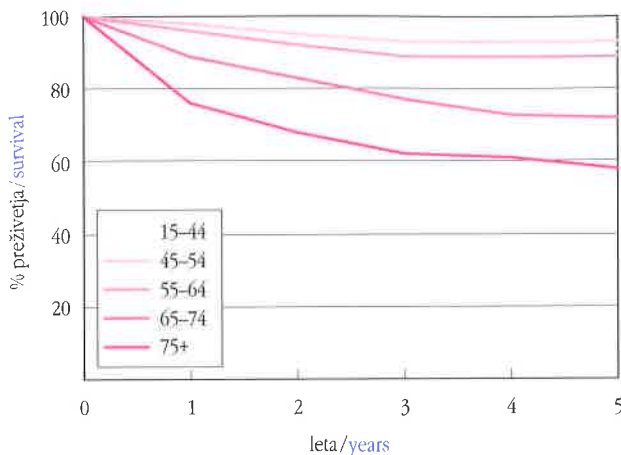
diated, 2% of patients received combined treatment of radiotherapy and chemotherapy, 3% received a combination of radiotherapy and hormonal therapy. Primary treatment was started at the Department of Obstetrics and Gynaecology, UMC in Ljubljana in 42% of patients, at the Institute of Oncology in Ljubljana in 25% of patients, in 10% of patients, it was started in the General Hospital in Maribor, in 7% in the General Hospital in Celje, in 3% in each of General Hospitals in Šempeter pri Novi Gorici, and Slovenj Gradec, in 2% in each of General Hospitals in Izola and Postojna, in 1% in each of General Hospitals in Kranj, Novo mesto, Jesenice, Ptuj and Trbovlje, and in 0.5% in each of General Hospitals in Brežice and in Murska Sobota.

The relative five-year survival rate was 5% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The survival improved in all patients with the disease at any stage (Figure 2). The survival of the patients younger than 65 years was by 19% higher than of patients 65-74 years old (Figure 3).

According to the EURO CARE-3 study results for the period 1990-94, in Europe, the age-standardized relative survival rate of the patients with the cancer of the corpus uteri was 73.4% (72.2-74.6), while in Slovenia, it was 72.8% (68.4-77.5). The highest rate of 81.1% was recorded in Tyrol in Austria.

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An increased incidence rate of the cancer of the corpus uteri did not have any influence upon the percentage of microscopically confirmed cases, which reached 99% and was consistent throughout the observation period. These data confirm the usefulness of the guidelines for the treatment of the cancer of corpus uteri that prescribe the diagnostic procedure in case of a suspected malignancy. The increasing incidence in elderly women, aged over 75 years, points to a more active diagnostic procedure and better preoperative management.



SLIKA 3: Relativno petletno preživetje bolnic z rakom materničnega telesa, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of corpus uteri cancer patients diagnosed in the period 1993–1997 by age.

pavzni krvavitvi oglasijo pri ginekologu. Določen doprinos pripišemo lahko tudi vedno pogostejši uporabi ultrazvočnih preiskav, predvsem vaginalnega ultrazvoka. Verjetno so abrazije maternične votline kot diagnostičen postopek indicirane pogosteje.

Izdaja doktrinarnih stališč Ginekološke klinike v Ljubljani, Onkološkega inštituta ter Ginekološko-porodniškega oddelka Splošne bolnišnice v Mariboru leta 1992 (1) je verjetno pripomogla k enotnejšemu načinu zdravljenja raka materničnega telesa in ne nazadnje h koncentriranju teh bolnic v naštetih treh ustanovah. Zdravljenje raka materničnega telesa se v zadnjih desetletjih ni bistveno spremenilo, postalo je celo nekaj manj agresivno, vsaj za večino pravočasno diagnosticiranih primerov bolezni. Kirurško zdravljenje je še vedno najbolj ustrezen način zdravljenja.

Še vedno pa ugotavljamo, da se 23% bolnic zdravi v drugih ustanovah in ne na Onkološkem inštitutu, Univerzitetni ginekološki kliniki v Ljubljani ter Ginekološkem oddelku Splošne bolnišnice Maribor. Poudarek, da so najboljši rezultati zdravljenja rakavih bolezni v centrih, kjer imajo največ izkušenj z zdravljenjem, se še ni uveljavil v celoti. Zdravljenje karcinoma materničnega telesa je v zgodnjih stadijih bolezni kirurško sicer manj zahtevno kot pri drugih ginekoloških rakih, vendar to ne opravičuje sedanjega stanja, saj se bodo izboljšani rezultati zdravljenja lahko pokazali v nadaljnjih obdobjih šele ob večjem upoštevanju doktrinarnih priporočil (2).

VIRA

1. Fras P, ed. Doktrina zdravljenja ginekoloških malignomov. Ljubljana: Onkološki inštitut, 1992.
2. Stržinar V, Baškovič M, Bebar S et al. Ginekološki malignomi: doktrina zdravljenja ginekoloških malignomov na Onkološkem inštitutu in Univerzitetni ginekološki kliniki. 2. rev. izd. Ljubljana: Zveza slovenskih društev za boj proti raku, 2001.

The increased five-year survival of the patients with regionally advanced disease in the period 1993–97 in comparison to the survival in the years 1983–87 is a proof that the post-operative treatment guidelines were observed.

Of the patients with the cancer of the corpus uteri, 77% received primary treatment at the Department of Obstetrics and Gynaecology, UMC in Ljubljana, at the Institute of Oncology in Ljubljana and at Department of Obstetrics and Gynaecology of the General Hospital in Maribor. Only 23% of these patients received primary treatment at other gynecological departments. In 4% of patients, it was impossible to apply specific treatment mainly because of the old age of the patients, advanced stage of the disease, and other comorbidities.

A 5% higher five-year survival in the period 1993–97 than that in the period 1983–87 may be due to earlier detection of the disease and higher awareness of postmenopausal women who visit the gynecologist as soon as they notice any bleeding. A contribution to the improved survival may also be a more frequent use of US examinations, in particular of the vaginal US. It is also very likely that curettage is more often indicated as diagnostic procedure.

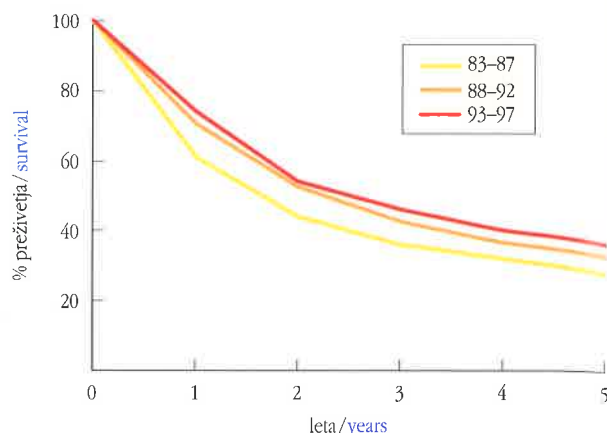
The publication of the «Guidelines for Treatment of Gynecological Cancers», edited in 1992 jointly by the following three central health care institutions, viz. Department of Obstetrics and Gynecology, UMC in Ljubljana, Institute of Oncology Ljubljana and Department of Obstetrics and Gynecology in the General Hospital in Maribor is an important contribution to a more standardized approach to the treatment of the cancer of the corpus uteri and to concentrating the patients with this cancer in the above three central health care institutions (1). The treatment of the cancer of the corpus uteri has not changed much in the recent decades; on the contrary, it has become even less aggressive in the cases in which the disease was diagnosed in time. Surgery has remained the treatment of choice for this cancer.

It has been observed that 23% of patients are still treated in health institutions other than the Institute of Oncology, Department of Obstetrics and Gynaecology, UMC in Ljubljana and Department of Obstetrics and Gynecology at the General Hospital in Maribor. The recommendations that the best treatment results are usually obtained in the health centers with most experiences in the treatment of a particular cancer, has not been fully brought into effect. The surgical treatment of the cancer of the corpus uteri in its early stage is not that demanding as the surgery of other gynecological cancers, nevertheless, this cannot justify the present treatment results. Their improvement will be noted in the years to come, after the recommendations contained in the «Guidelines for Treatment of Gynecological Cancers» will have been strictly followed (2).

JAJČNIK

OVARY

MKB 8 / ICD 8: 1830



SLIKA 1: Relativno petletno preživetje bolnic z žleznim karcinomom jajčnikov, zbolelih v letih 1973–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of ovarian adenocarcinoma patients diagnosed in the period 1973–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom jajčnikov 2399 bolnic, od tega v letih 1993–97 906. V analizo ni bilo vključenih 167 (7%) bolnic, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka jajčnikov večala. V letih 1983–87 je bila groba incidenčna stopnja 13,7/100.000 žensk, v letih 1993–97 pa 17,7/100.000 žensk. V zadnjem obdobju so bile vključene tudi bolnice z mejno malignimi tumorji. Mejno maligni tumorji so bili vključeni v redno registracijo raka šele leta 1991. V letih 1991–92 jih je bilo 46, v letih 1993–97 pa 128.

Odstotek mikroskopsko potrjenih primerov se je povečal s 94% v letih 1983–87 na 97% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 92% adenokarcinomov (od tega 16% mejno malignih), 4% neopredeljenih karcinoma.

In the period 1983–97, a total of 2,399 female patients were diagnosed with the ovarian cancer; of these, 906 females were diagnosed with this cancer in the period 1993–97. In 167 patients (7%), ovarian cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of the ovarian cancer was increasing. In the period 1983–87, the crude incidence rate was 13.7/100,000 females, whereas in 1993–97, it was 17.7/100,000 females. The tumors with borderline malignancy have been regularly registered only since 1991. In the period 1991–92, 46 cases were registered and, in 1993–97, 128.

In comparison to the observation period 1983–87, the percentage of microscopically confirmed cases increased by 3% in the observation period 1993–97, i. e. from 94% to 97%. In the

TABELA 1a: Jajčnik, žlezni karcinomi. Bolnice vključene v analizo po starosti in obdobju opazovanja.

TABLE 1a: Ovary, adenocarcinoma. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Ženske Females	1983-87	495	0	52	127	162	105	49
	1988-92	602	0	75	134	194	123	76
	1993-97	615	1	63	131	182	160	78

TABELA 2a: Jajčnik, žlezni karcinomi. Bolnice vključene v analizo po stadiju bolezni in obdobju opazovanja.

TABLE 2a: Ovary, adenocarcinoma. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%				
Ženske Females	1983-87	495	64	12,9	83	17,0	342	69,1	6	1,0
	1988-92	602	95	15,8	74	12,3	428	71,1	5	0,8
	1993-97	615	100	16,2	84	13,7	426	69,3	5	0,8

TABELA 1b: Jajčnik, mejno maligni. Bolnice vključene v analizo po starosti in obdobju opazovanja.

TABLE 1b: Ovary, borderline. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Ženske Females	1983-87	0	0	0	0	0	0	
	1988-92	46	0	18	9	12	4	3
	1993-97	128	0	48	27	24	17	12

TABELA 2b: Jajčnik, mejno maligni. Bolnice vključene v analizo po stadiju bolezni in obdobju opazovanja.

TABLE 2b: Ovary, borderline. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%				
Ženske Females	1983-87	0	0	0	0	0	0	0		
	1988-92	46	35	76,0	4	8,6	7	15,2	0	0,0
	1993-97	128	97	75,8	13	10,2	17	13,3	1	0,8

TABELA 3: Jajčnik, žlezni karcinomi. Opazovano in relativno petletno preživetje po obdobju opazovanja s 95 % intervalom zaupanja (IZ).**TABLE 3: Ovary, adenocarcinoma. Observed and relative five-year survival by period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano/Observed (%)					
	Ženske/Females					
	Leta/Years		Leta/Years		Leta/Years	
	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	60	(54-66)	34	(30-38)	25	(21-29)
1988-92	69	(65-73)	40	(36-44)	33	(29-37)
1993-97	73	(69-77)	43	(39-47)	33	(29-37)

Obdobje/ Period	Relativno/Relative (%)					
	Ženske/Females					
	Leta/Years		Leta/Years		Leta/Years	
	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	61	(56-66)	36	(31-41)	28	(24-32)
1988-92	71	(67-75)	42	(38-46)	33	(29-37)
1993-97	74	(70-78)	46	(42-50)	37	(23-41)

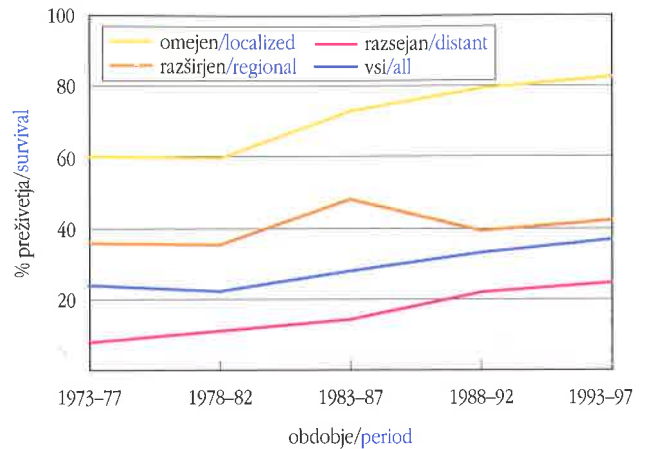
mov in 3% malignomov kličnih celic ter posamezni primeri malignega granuloceličnega tumorja in malignega tekoma.

Starostna porazdelitev v analizo zajetih bolnic z invazivnim žleznim karcinomom se je spremenila. V letih 1993-97 je bilo več bolnic starih 65-74 let. Med bolnicami z mejno malignimi tumorji pa je bilo največ mladih, starih 15-44 let (tabela 1). Razširjenost bolezni ob diagnozi invazivnih žleznih karcinomov se ni pomembno spremenila. V letih 1993-97 je bila še vedno pri 69% bolnic odkrita že razsejana bolezen. Med mejno malignimi pa je bilo največ omejene bolezni (tabela 2).

V letih 1993-97 je bilo specifično zdravljenih 91% vseh bolnic. Prvo zdravljenje je bilo v 56,5% kirurško in citostatsko, v 25% samo kirurško, v 10% samo citostatsko, v 5,5% kirurško, obsevalno in citostatsko in v 1% kirurško in obsevalno. Prvo zdravljenje se je pričelo v 35% na Ginekološki kliniki v Ljubljani, v 25% na Onkološkem inštitutu v Ljubljani, v 13% v SB v Mariboru, v 6% v SB v Celju, po 4% v SB v Šempetru pri Novi Gorici in Slovenj Gradcu, po 3% v SB v Novem mestu in Izoli, po 2% v bolnišnici v Kranju in v SB na Jesenicah, po 1% pa v SB v Trbovljah in na Ptujju. V manj kot 1% so bile bolnice zdravljene v SB v Brežicah in v Postojni.

Če upoštevamo samo invazivne žlezne karcinome, je bilo v letih 1993-97 relativno petletno preživetje za 9% večje kot v letih 1983-87 (slika 1, tabela 3). Povečalo se je pri bolnicah v vseh stadijih bolezni, največ pa pri bolnicah z razsejano boleznijo (slika 2). Pri bolnicah, mlajših od 55 let je bilo za 24% večje kot pri starih 65 let in več (slika 3). Pri bolnicah z mejno malignimi tumorji pa je bilo preživetje 96% (slika 4).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka jajčnikov 31,9% (30,9-32,9), v Sloveniji 31,4% (27,3-36,2). Največje preživetje je bilo 46% na Islandiji.

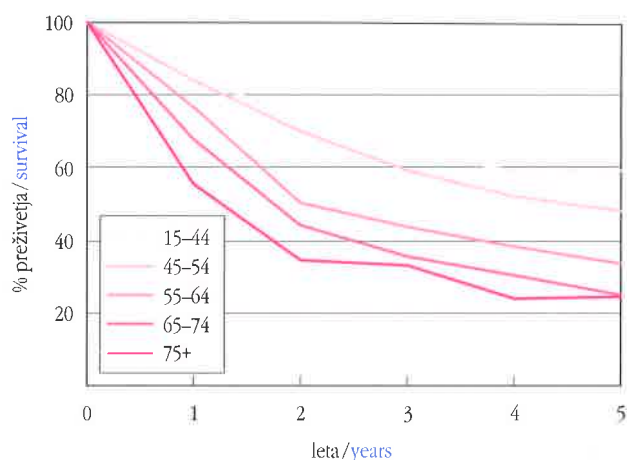
**SLIKA 2: Relativno petletno preživetje bolnic z žleznim karcinomom jajčnikov, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.****FIGURE 2: Relative five-year survival of ovarian adenocarcinoma patients diagnosed in the period 1973-1997 by stage and period of diagnosis.**

years 1993-97, the percentage of adenocarcinomas, non-specified carcinomas, and other germ cell malignancies in the microscopically confirmed cases was 92% (of these, 16% with borderline malignancy), 4%, and 3%, respectively. There were also some cases of granulosa-cell malignant tumors and malignant thecomas.

The age distribution of patients with invasive adenocarcinoma included into the analysis has been changing (Table 1). In the period 1993-97, a higher number of patients of the age group of 65-74 years were included in the analysis. In the group of patients with tumors with borderline malignancy, younger patients, aged between 15-44 years, prevailed. The stage distribution of invasive adenocarcinomas at diagnosis did not significantly change (Table 2). Among the cases of borderline malignancies, the localized disease prevailed.

In the period 1993-97, 91% of patients underwent specific treatment. Surgery in combination with chemotherapy was applied as primary treatment in 56.5% of patients, 25% of patients underwent surgery alone, 10% received chemotherapy alone, 5.5% of patients received combined treatment of surgery, radiotherapy and chemotherapy, and 1% received a combination of surgery and radiotherapy. Primary treatment was started at the Department of Obstetrics and Gynaecology, UMC in Ljubljana in 35% of patients, at the Institute of Oncology in Ljubljana in 25% of patients, in 13% of patients, it was started in the General Hospital in Maribor, in 6% in the General Hospital in Celje, in 4% in each of General Hospitals in Šempeter pri Novi Gorici, and Slovenj Gradec, in 3% in each of General Hospitals in Novo mesto and in Izola, in 2% in each of General Hospitals in Kranj, and Jesenice, in 1% in each of General Hospitals in Trbovlje and in Ptuj, and in less than 1% in each of General Hospitals in Brežice and in Postojna.

The relative five-year survival rate of the patients with invasive adenocarcinoma was 9% higher in the years 1993-97 than in the years 1983-87 (Figure 1, Table 3). The survival improved



SLIKA 3: Relativno petletno preživetje bolnic z žleznim karcinomom jajčnikov, zbolelih v letih 1993–97 po starosti.

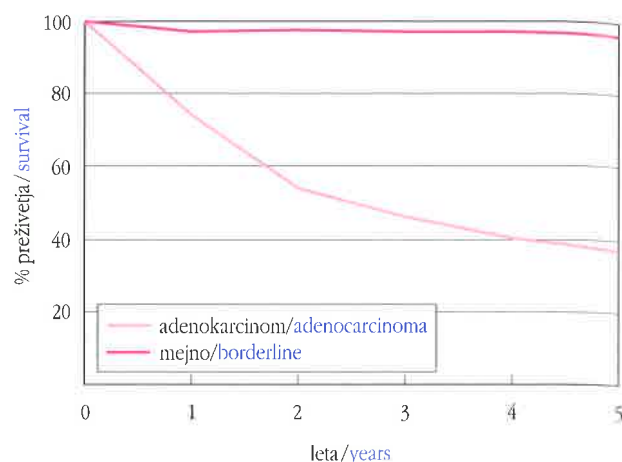
FIGURE 3: Relative five-year survival of ovarian adenocarcinoma patients diagnosed in the period 1993–1997 by age.

Marjetka Uršič - Vrščaj, Onkološki inštitut Ljubljana

Pri podrobni analizi podatkov za obdobje od leta 1983–97 je potrebno upoštevati delež mejno malignih tumorjev, ki so v gradivo priključeni šele od leta 1991, predvsem zaradi klinično pomembno drugačnega poteka bolezni kot pri invazivnih adenokarcinomih jajčnikov (slika 4). Za klinično uporabo je bolj primeren in pogostejše uporabljen izraz, tudi v tuji literaturi, tumorji nizke stopnje malignosti – izraz mejno maligni tumorji namreč lahko zavaja k neustreznim ukrepom, ki veljajo predvsem za nadzor bolnic po zdravljenju. Bolnice z mejno malignimi tumorji jajčnikov so večinoma mlajše od 50 let, z večjim deležem omejene bolezni ob diagnozi, z obnovitvijo bolezni po 10 letih in kasneje in boljšim preživetjem.

Večji odstotek mikroskopsko potrjenih rakov jajčnikov (za 3%), manjši odstotek patohistološko neopredeljenih rakov jajčnikov (za 9%), manjši odstotek neznanega stadija (za 3%) in nekoliko večji odstotek omejenega stadija pri invazivnih adenokarcinomih (za 3,5%) kažejo na izboljšanje diagnostičnih postopkov pri odkrivanju raka jajčnikov v letih 1993–97. Izboljšanje diagnostičnih postopkov temelji na izboljšanju in bolj množični uporabi nekaterih ključnih diagnostičnih metod za odkrivanje raka jajčnikov (pogostejši uporabi abdominalnega in vaginalnega ultrazvoka ter uvajanju določevanja CA 125 kot osnovnega tumorskega označevalca za raka jajčnikov, predvsem v ginekoloških in splošnih ambulantah). Zelo verjetno pa so ugodni podatki tudi odraz boljše ozaveščenosti žensk o zgodnjih znakih bolezni in nenazadnje večjega strokovnega znanja na tem področju pri ginekologih in drugih zdravnikih ne-onkologih.

Povečanje preživetja bolnic z žleznim karcinomom v obdobju 1988–97 odraža več dejavnikov, ki pomembno vplivajo na preživetje bolnic: večji delež optimalno radikalno operiranih bolnic (citoredukcija tumorskih mas z ostankom manj kot 0,5 cm v premeru največjega ostanka oz. po novem 0–1 g tumorskega tkiva, kar odgovarja približno 1 × 1 cm celokupnega



SLIKA 4: Relativno petletno preživetje bolnic z rakom jajčnikov, zbolelih v letih 1993–1997 po histološki vrsti.

FIGURE 3: Relative five-year survival of ovarian cancer patients diagnosed in the period 1973–1997 by hystology.

in all disease stages, with the improvement being the highest in the patients with advanced disease (Figure 2). The survival of the patients younger than 55 years was 24% higher than that of the patients aged over 65 years (Figure 3). In the patients with the tumors with borderline malignancy, the survival was 96% (Figure 4).

According to the EUROCARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with ovarian cancer was 31.9% (30.9–32.9), while in Slovenia, it was 31.4% (27.3–36.6). The highest rate of 46% was recorded in Iceland.

Marjetka Uršič - Vrščaj, Institute of Oncology Ljubljana

A close analysis of the period 1983–97 should also take into consideration the percentage of tumors with borderline malignancy that were included into the study only in 1991, mainly on account of its course of disease that is different from that of invasive adenocarcinoma of the ovaries (Figure 4). In clinical terminology, these tumors are usually termed as tumors with low malignancy grade. The term 'borderline malignancy' may be in fact misleading, actually making us apply inappropriate treatment measures that are normally applied in the follow-up of the patients after the therapy. The patients with ovarian tumors of borderline malignancy are usually younger than 50 years. At diagnosis, a higher percentage of patients with localized disease is observed. After 10 or more years, recurrence of the disease may develop. Even so, their survival is better.

The 3% higher percentage of microscopically confirmed ovarian cancers, 9% lower percentage of patohistologically non-specified ovarian cancers, 3% lower percentage of tumors with unknown stage and 3.5% higher percentage of invasive adenocarcinomas in its localized stage are the data that indicate to an improvement of diagnostic procedures for ovari-

ostanka tumorske mase) pred kemoterapijo ali najkasneje po štirih krogih citostatikov (rezultati drugih raziskav na Onkološkem inštitutu) in uvajanje novih citostatikov (1). Delež izvršenih operacij v večjih centrih (Ginekološka klinika, Onkološki inštitut, Maribor, Celje, Nova Gorica) je v zadnjem obdobju za 8% večji. To je pomemben podatek, saj je znano, da je delež uspešno, radikalno, izvršenih operacij večji v izurjenih centrih (60–90%) kot v manjših, strokovno manj izurjenih bolnišnicah (20–30%). Večji delež po sodobnih strokovnih kriterijih kvalitetnejše operiranih bolnic odraža tudi boljše strokovno znanje operaterjev o nujnosti čim bolj radikalnih primarnih operacij v sklopu celovitega zdravljenja raka jajčnikov.

Olga Cerar, Onkološki inštitut Ljubljana

Povečanje relativnega petletnega preživetja za 9% je tudi rezultat primernejšega sistemskega zdravljenja. V letih 1993–97 so bile že vse bolnice zdravljene s preparati platine, v prejšnjih letih pa ne. Prav tako je bilo sistemsko zdravljenje uporabljeno v primarnem zdravljenju v večjem odstotku (72%), saj obsevanje ni več pomembno. Začeli smo uvajati nove citostatike, v letu 1996 taksane. Tudi možnosti dodatne kemoterapije so bile večje in večkrat uporabljene (2).

VIRA

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an cancer achieved in the period 1993–97. This improvement was due to a more advanced and frequent use of some key diagnostic procedures in the ovarian cancer detection in gynecological and general outpatient departments, viz. abdominal US, vaginal US, determination of CA125, the tumor marker for ovarian cancer. These encouraging data may also reflect a higher awareness of women of early cancer symptoms and better knowledge and experience of specialists in gynecology in this field as well as of other physicians, not specialized in oncology.

The improved survival of the patients with adenocarcinoma observed in the years 1988–97 is the result of several factors influencing significantly the survival. These are: higher proportion of patients optimally treated by radical surgery (cytoreduction of the tumor mass with the residue of less than 0.5 cm in diameter or, according to new standards, with the residue not exceeding 0–1 g of tumor tissue, which matches the overall residue of tumor mass of the size 1 × 1 cm) before chemotherapy or after four cycles of chemotherapy at the latest and application of new cytostatics (1). The percentage of patients treated surgically in larger health centers (at the Department of Obstetrics and Gynaecology, UMC in Ljubljana, at the Institute of Oncology in Ljubljana, at General Hospitals in Maribor, Celje, and in Sempeter pri Novi Gorici) increased by 8% in the last observation period. These data are extremely important since it is generally recognized that radical surgical interventions are as rule more successful if performed in larger health centers with more skilled personnel (60–90%) than in smaller ones (20–30%). A considerably higher percentage of ovarian cancer patients who underwent high quality surgical treatment is a strong argument in favor of the extended knowledge and skills of our gynecologists and of their awareness that, within the treatment plan for ovarian cancer, primary surgery as radical as possible is indispensable.

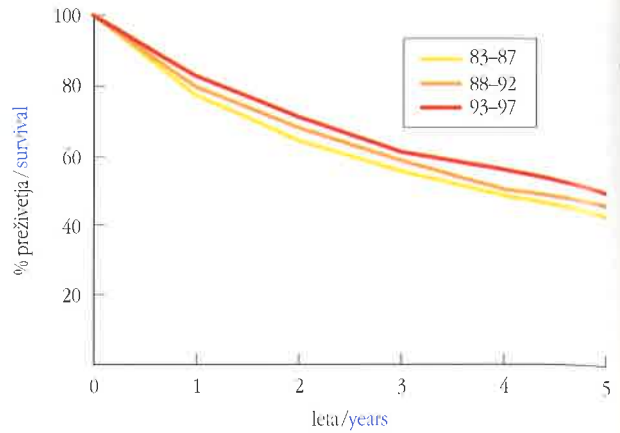
Olga Cerar, Institute of Oncology Ljubljana

A 9-percent increase of the relative five-year survival is also due to more appropriately planned systemic treatment. In the years 1993–97, all patients were treated with platinum drugs in contrast to the patients from earlier periods who never received these drugs. Moreover, systemic treatment was more frequently, in 72% of patients, applied as primary treatment, and irradiation has lost its importance. It should be noted that, in 1996, new cytostatics, viz. taxanes, were introduced into clinical practice. The availability of salvage chemotherapy was greater and was therefore applied more frequently (2).

PROSTATA

PROSTATE

MKB 8/ICD 8: 185



SLIKA 1: Relativno petletno preživetje bolnikov z rakom prostate, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of prostate cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom prostate 4108 bolnikov, od tega v letih 1993–97 1730. V analizo ni bilo vključenih 424 (10%) bolnikov, ker je bil pri njih rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka prostate zelo povečala. V letih 1983–87 je bila groba incidenčna stopnja 23,9/100.000 moških, v letih 1993–97 pa 36/100.000 moških.

Odstotek mikroskopsko potrjenih primerov se je povečal s 83% v letih 1983–87 na 87% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 74% adenokarcinomov, 25% neopredeljenih karcinomov in posamezni primeri prehodnoceličnega, ploščatoceličnega in drobnooceličnega karcinoma.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnikov v starosti 55–74 let. Razširjenost bolezni ob diagnozi se je spremenila. Odstotek neznanega stadija se je zmanjšal, odstotek razširjene bolezni pa nekoliko povečal (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 92% bolnikov. Prvo zdravljenje je bilo v 36% kirurško in hormonsko, v 28% samo kirurško, v 26% samo hormonsko, v 3% obsevalno in hormonsko, v 2% kirurško, obsevalno in hormonsko, v 2% kirurško in ali samo obsevalno, v 2% so bolniki dobili tudi kemoterapijo. Prvo zdravljenje se je pričelo v 30% na Kliničnem oddel-

In the period 1983–97, a total of 4,108 patients were diagnosed with the prostate cancer; of these, 1,730 males were diagnosed with this cancer in the period 1993–97. In 424 patients (10%), prostate cancer was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of the prostate cancer increased considerably. In the period 1983–87, the crude incidence rate was 23.9/100,000 males, whereas in 1993–97, it was 36/100,000 males.

In comparison to the observation period 1983–87, the percentage of microscopically confirmed cases increased by 4% in the observation period 1993–97, i. e. from 83% to 87%. In the years 1993–97, the percentage of adenocarcinomas and non-specified carcinomas in the microscopically confirmed cases was 74% and 25%, respectively. There were also some cases of transitional-cell, squamous-cell and small-cell carcinomas.

The age distribution of patients included into the analysis has been changing (Table 1). In the period 1993–97, a higher number of patients of the age group of 55–74 years were included in the analysis. The stage distribution at diagnosis changed. The percentage of cases of unknown stage declined, whereas the percentage of regional disease slightly increased (Table 2).

In the period 1993–97, 92% of patients underwent specific treatment. Surgery in combination with hormonal therapy was

TABELA 1: Prostata. Bolniki vključeni v analizo po starosti in obdobju opazovanja.

TABLE 1: Prostate. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87 1988-92 1993-97	995 1134 1555	0 0 0	1 2 7	23 30 43	130 173 266	353 374 702	488 555 537

TABELA 2: Prostata. Bolniki vključeni v analizo po stadiju bolezni in obdobju opazovanja.

TABLE 2: Prostate. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage							
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%	%	%	%
Moški Males	1983-87 1988-92 1993-97	519 511 781	52,2 45,1 50,2	89 111 211	8,9 9,8 13,6	195 249 319	19,6 22,0 20,5	192 263 244	19,3 23,2 15,7

TABELA 3: Prostata. Opazovano in relativno petletno preživetje po obdobju opazovanja s 95 % intervalom zaupanja (IZ).**TABLE 3: Prostate. Observed and relative five-year survival by period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano / Observed (%)					
	1		3		5	
	IZ/CI		IZ/CI		IZ/CI	
1983-87	71	(68-74)	43	(40-46)	28	(25-31)
1988-92	74	(71-77)	46	(43-49)	30	(27-33)
1993-97	77	(75-79)	49	(46-52)	35	(32-38)

Obdobje/ Period	Relativno / Relative (%)					
	1		3		5	
	IZ/CI		IZ/CI		IZ/CI	
1983-87	77	(74-80)	56	(52-60)	43	(39-47)
1988-92	80	(77-83)	59	(55-63)	47	(43-51)
1993-97	83	(81-85)	61	(58-64)	50	(46-54)

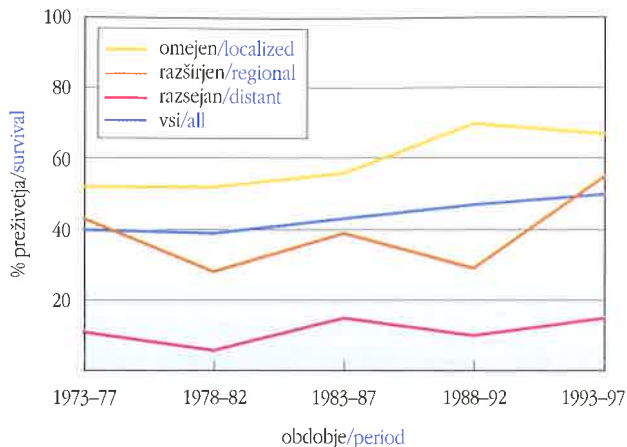
ku za urologijo KC v Ljubljani, v 16 % v SB v Mariboru, v 12 % v SB v Celju, v 8 % v SB v Slovenj Gradcu, po 7 % v SB v Novem mestu in v Murski Soboti, v 6 % v SB v Šempetru pri Novi Gorici, v 3 % v SB v Izoli, po 2 % v SB na Jesenicah, pri zasebnih zdravnikih in na drugih kliničnih oddelkih KC. Na Onkološkem inštitutu v Ljubljani pa je pričelo prvo zdravljenje 5 % bolnikov.

V letih 1993-97 je bilo relativno petletno preživetje za 7 % večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo pri bolnikih z omejeno in razširjeno boleznijo. Preživetje je bilo največje pri bolnikih, starih 55-74 let. Pri bolnikih mlajših od 55 let je bilo preživetje manjše samo dve leti po diagnozi, po petih letih pa je bilo manjše le pri najstarejši skupini bolnikov (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka prostate 61,5 % (59,8-63,2), v Sloveniji 47,3 % (38,4-58,2). Največje preživetje je bilo 83,6 % na Tirolskem v Avstriji.

Andrej Kmetec, Klinični oddelek za urologijo KC

Ob rastoči incidenci se kaže pomik proti srednji življenjski dobi. K temu je pripomogla hitrejša in bolj natančna diagnostična obdelava, po drugi strani pa tudi boljša ozaveščenost moških. Bolniki prej obiščejo urologa zaradi težav ali pa zaradi preventivnih razlogov. Rak prostate, ko je omejen na samo prostato, le redko povzroča težave v smislu znamenj obstrukcije ali draženja spodnjih sečil, v kolikor ni istočasno prisotno še benigno povečanje prostate. Šele pri lokalno razširjeni ali razsejani bolezni se lahko pojavijo dizurične težave. Tako si lahko tudi razlagamo porast odstotka razširjene oblike bolezni. Sum na raka prostate se navadno postavi na osnovi tumorskega označevalca serumskega prostatičnega specifičnega antigena (PSA), dokončno potrditev pa omogoča transrektalna ultrazvočna preiskava z biopsijo prostate. Čeprav je digitorek-

**SLIKA 2: Relativno petletno preživetje bolnikov z rakom prostate, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.****FIGURE 2: Relative five-year survival of prostate cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.**

applied as primary treatment in 36% of patients, 28% of patients underwent surgery alone, 26% received hormonal therapy alone, 3% received radiotherapy and hormonal therapy, 2% received surgery, radio- and hormonal therapy, 2% of patients received surgery and/or radiotherapy alone, and 2% received also chemotherapy.

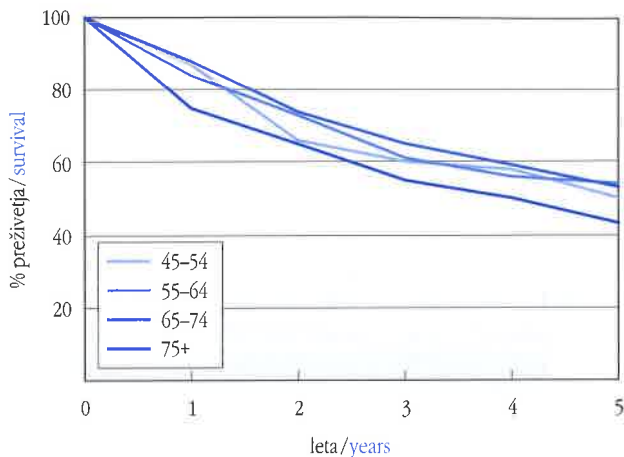
Primary treatment was started at the Department of Urology, UMC in Ljubljana in 30% of patients, in the General Hospital in Maribor in 16% of patients, in 12% in the General Hospital in Celje, in 8% in the General Hospital in Slovenj Gradec, in 7% in each of General Hospitals in Novo mesto and in Murska Sobota, in 6% in Šempeter pri Novi Gorici, in 3% in the General Hospital in Izola, in 2% in the General Hospital in Jesenice and in private health institutions as well as other departments at UMC in Ljubljana. At the Institute of Oncology, primary treatment was started in 5% of prostate cancer patients.

The relative five-year survival rate of the patients with invasive adenocarcinoma was 7% higher in the years 1993-97 than in the years 1983-87 (Figure 1, Table 3). The survival improved in the patients with localized and regional diseases. The highest survival was observed in the patients aged between 55-74 years. In the patients younger than 55 years, the survival slightly decreased two years after the diagnosis, whereas five years after the diagnosis, it was lower only in the oldest group of patients (Figure 3).

According to the EURO CARE-3 study results for the period 1990-94 in Europe, the age-standardized relative survival rate of the patients with prostate cancer was 61.5% (59.8-63.2), while in Slovenia, it was 47.3% (38.4-58.2). The highest rate of 83.6% was recorded in Tyrol in Austria.

Andrej Kmetec, Department of Urology, UMC, Ljubljana

The highest increase of prostate cancer incidence is observed in the patients of middle years. This is attributable to more rapid and accurate diagnostic procedures on the one hand, and on



SLIKA 3: Relativno petletno preživetje bolnikov z rakom prostate, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of prostate cancer patients diagnosed in the period 1993–1997 by age.

talni pregled še vedno osnovna preiskava bolnika, pa z njo le redko lahko posumimo na začetno obliko raka prostate. Ob tem se postavlja vprašanje, katera je tista vrednost PSA, ko se je potrebno odločiti za transrektalno ultrazvočno preiskavo in biopsijo prostate neglede na težave bolnika. Večina avtorjev danes meni, da je ta vrednost nad 3 ng/ml. S tem pa ni rečeno, da nižje vrednosti izključujejo možnost raka prostate. Vsaka povišana vrednost PSA še ne pomeni, da gre za raka prostate, saj se višje vrednosti pojavijo tudi pri drugih boleznih prostate. Potrebno je ponavljati oziroma spremljati hitrost porasta vrednosti PSA v nekem časovnem obdobju (1).

V Sloveniji potekajo poleg rednih tudi preventivni pregledi in presejanje moških zaradi bolezni prostate, zlasti tistih po 50. letu starosti. S tem želimo zajeti čim več moških z rakom prostate v začetnem obdobju.

Danes je osnovno zdravljenje raka prostate kirurško. Radikalna prostatektomija, kjer se poleg celotne prostate odstranijo še bezgavke in semenski mešički, zagotavlja po mnenju večine avtorjev, v kolikor je bolezen omejena na organ, ozdravljenje. Število teh posegov vsako leto, vse od leta 1992 narašča, saj je možno ugotoviti tudi vse več bolnikov z boleznijo, ki je omejena na prostato. Hormonsko zdravljenje se uveljavlja kot dodatno pred- ali pooperativno zdravljenje in tam, kjer gre za razširjeno ali razsejano obliko bolezni. Osnovni namen je odtegnitev hormona testosterona rakastim celicam prostate (2, 3, 4).

Transuretralna resekcija je pri raku prostate indicirana le v primeru, ko pri napredovani obliki bolezni, potem ko je uvedeno sistemsko zdravljenje, pride do obstrukcije spodnjih sečil. Takšen poseg ima lahko za posledico pogoste krvavitve iz sečnice ali pa pospeši razsoj bolezni, zato se tovrstnim posegom pri raku prostate izogibamo.

Radikalno obsevanje prostate kot primarno zdravljenje se izvaja le v redkih primerih, zlasti kadar splošno stanje bolnika ne dopušča bolj agresivnega pristopa do bolezni. V svetu se uveljavlja tudi metoda vsajanja drobnih radioaktivnih delcev v samo tkivo prostate ob ultrazvočni kontroli.

the other, also to higher awareness of men of the risk of this cancer. The patients more often visit the urologist for the disorders they observe or for preventive reasons. The prostate cancer in its localized stage only occasionally causes obstructions or irritations in the inferior urinary tract, particularly if a concomitant benign enlargement of the prostate develops. Serious diuretic disorders usually occur in locally advanced and metastatic disease. This may also explain the increased percentage of the patients with regional stage of the disease. The prostate cancer is suspected on the basis of the prostate-specific antigen (PSA), where final confirmation of the suspected cancer may be obtained by transrectal US examination in combination with biopsy of the prostate. Though the digitorectal examination of the prostate remains the primary examination method, it hardly ever casts suspicion to an early prostate cancer. At this point, we should need to know which PSA value is crucial and indicative to perform transrectal US and biopsy of the prostate, irrespective of the troubles the patient has. The majority of authors believe that this crucial value is 3 ng/ml, which does not suggest that lower values than that exclude the possibility of cancer and that each increased value of PSA is indicative of cancer because PSA may rise also in other diseases of the prostate. In any patient with an increased PSA value, the rate of increase should be followed-up for a certain period of time (1).

In addition to regular examinations in Slovenia, preventive examinations and screening of men over 50 years old for the diseases of the prostate are being held. This is the only promising way that allows detecting as much cases of this cancer as possible in its early stage.

Surgery is considered to be the primary treatment of choice for the prostate cancer. Radical prostatectomy that removes, besides the complete prostate, also the lymph nodes and seminal vesicles, is curative if the disease is localized. The number of these surgical interventions has been increasing since 1992 with the growing number of the patients in whom the disease was diagnosed as localized to the prostate. Hormonal treatment is being applied as adjuvant pre- or post-operative therapy and in the patients with advanced disease. The principle of hormonal treatment is based on withdrawing testosterone from cancer cells (2, 3, 4).

Transurethral resection is indicated only in advanced disease if the lower urinary tract is obstructed. The side effects of this surgery may be frequent bleeding from the urethra and more rapid metastatic spread of the disease. This method is therefore often avoided.

Radical radiotherapy of the prostate is rarely performed as primary treatment and particularly not in cases when general physical condition of the patient does not allow any aggressive treatment approach. Recently, brachytherapy by US-guided implantation of small radioactive particles into the prostate tissue has been introduced.

In the observation period 1983–97, the five-year survival improved. With screening using PSA value assessment and other preventive examinations for the detection of prostate cancer in men over 50 years old we were successful in finding more patients with the disease in early stage and also cured them.

Petletno preživetje se je v opazovanem obdobju 1983–97 povečalo. Glede na to, da smo uvedli dokaj široko presejanje moških po 50. letu starosti z določanjem PSA in s preventivnimi pregledi, menim, da lahko s tako široko aktivnostjo odkrijemo večje število bolnikov z začetno obliko bolezni in jih tudi ozdravimo.

Koliko bomo uspešni pri tej široko zastavljeni aktivnosti odkrivanja in zdravljenja, nam bo pokazalo naslednje obdobje opazovanja.

France Marolt, Onkološki inštitut Ljubljana

Še vedno preseneča premajhno število mikroskopsko potrjenih primerov. Večji odstotek mlajših si lahko razložimo s široko uporabo PSA v zadnjem obdobju tudi v Sloveniji. V začetku 90. let je bilo na voljo tudi večje število diagnostičnih preiskav za natančno zamejitev bolezni. Zato je bil večji odstotek bolezni opredeljen kot razširjen.

Preseneča velik odstotek bolnikov, ki so bili zdravljeni hormonsko in majhen odstotek obsevanih. Tudi pri raku prostate bi bil na mestu multidisciplinaren pristop že v času prvega zdravljenja (5). Takšnega pristopa zaenkrat v Sloveniji še ni. Stanje je praktično enako stanju ob koncu 80. let. Preživetje bi se lahko izboljšalo z boljše planiranim prvim zdravljenjem, z boljšo diagnostiko, z nadaljnjim razvojem kirurgije in oblikovanjem skupinskega pristopa, kot je na primer pri raku ščitnice in rakah glave in vratu.

We will be able to evaluate the effect of this wide range of activities related to the detection and treatment of the prostate cancer only in the analyses of the next observation period.

France Marolt, Institute of Oncology Ljubljana

A small number of microscopically confirmed cases of the prostate cancer is rather surprising. An increased number of detected prostate cancer cases in younger men may be attributed to the recent widely used PSA determination in Slovenia. In the early 1990s, more diagnostic techniques were available for the disease staging, which can also explain why a higher percentage of cases was staged as regional disease.

At the same time, the data showing a considerably high percentage of patients who received hormonal therapy and rather low percentage of irradiated patients are also startling. In the treatment of prostate cancer, a multidisciplinary approach should have been applied already in planning primary treatment (5). Such an approach has not yet been established. The situation today is much the same as it was by the end of the 1980s. The survival could have been better with a more sensible planning of primary treatment, with better diagnostics, with further advances in surgery and establishing a team approach to the treatment of prostate cancer, as it has been introduced in the treatment of thyroid, and head and neck cancers.

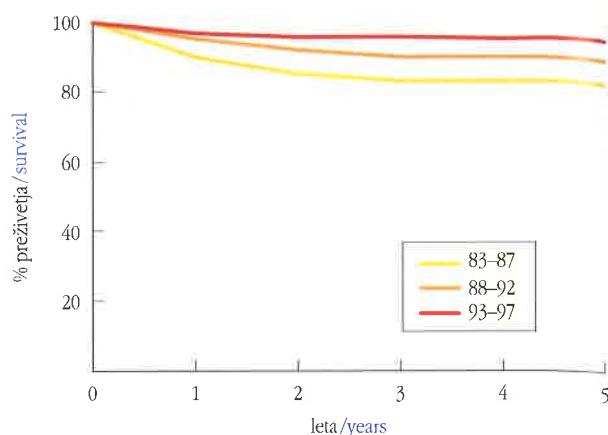
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MODO

TESTIS

MKB 8 / ICD 8: 186



SLIKA 1: Relativno petletno preživetje bolnikov z rakom moda, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of testicular cancer patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom moda 785 bolnikov, od tega v letih 1993–97 335. V analizo ni bil vključen 1 bolnik, ker je bil pri njem rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka moda večala. V letih 1983–87 je bila groba incidenčna stopnja 4,4/100.000 moških, v letih 1993–97 pa 7/100.000 moških.

Odstotek mikroskopsko potrjenih primerov se je povečal s 87% v letih 1983–87 na 93% v letih 1993–97. Med mikroskopsko potrjenimi je bilo v letih 1993–97 45% seminomov, 46% drugih malignomov kličnih celic (embrionalni karcinomi, tumorji rumenjakeve vrečke, teratokarcinomi in mešani tumorji), 6% horiokarcinomov, 3% ne-Hodgkinovih limfomov in en primer hemangiosarkoma.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnikov v starosti 15–44 let. Razširjenost bolezni ob diagnozi se je spremenila. V zadnjem obdobju je bilo zaradi natančnejše diagnostike več bolnikov z razširjeno boleznijo ob diagnozi. Z razsejano boleznijo pa je bilo odkritih manj bolnikov (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 99% bolnikov. Prvo zdravljenje je bilo v 63% kirurško in citostatsko, v 21% samo kirurško in v 15% kirurško in obsevalno in v 1% kirurško, citostatsko in obsevalno. Prvo zdravljenje se je pričelo v 53% na Kliničnem oddelku za urologijo KC v Ljubljani, po 9% v SB v Mariboru in Celju, v 7% v SB v Slovenj Gradcu, v 6%

In the period 1983–97, a total of 785 patients were diagnosed with the testicular cancer; of these, 335 males were diagnosed with this cancer in the period 1993–97. In 1 patient, testicular cancer was diagnosed at death; therefore, he was not included in the analysis.

In the observed 15-year period, the incidence of testicular cancer was increasing. In the period 1983–87, the crude incidence rate was 4.4/100,000 males, whereas in 1993–97, it was 7/100,000 males.

In comparison to the observation period 1983–87, the percentage of microscopically confirmed cases increased by 6% in the observation period 1993–97, i. e. from 87% to 93%. In the years 1993–97, the percentage of seminomas, of other germ cell malignancies (embryomas, yolk sac tumors, teratocarcinomas and mixed tumor types), choriocarcinomas, and non-Hodgkin lymphomas in the microscopically confirmed cases was 45%, 46%, 6% and 3%; there was one case of hemangiosarcoma.

The age distribution of patients included into the analysis has been changing (Table 1). In the period 1993–97, a higher number of patients of the age group of 15–44 years were included in the analysis. The stage distribution at diagnosis changed, too. The increase of the percentage of patients with regional disease at diagnosis was due to more accurate diagnostic techniques, whereas the number of the patients with metastatic disease was considerably lower (Table 2).

TABELA 1: Moda. Bolniki vključeni v analizo po starosti in obdobju opazovanja.

TABLE 1: Testis. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
		-14	15–44	45–54	55–64	65–74	75+
Moški Males	1983–87 204	3	172	21	5	1	2
	1988–92 247	2	205	17	15	4	4
	1993–97 333	3	293	20	9	6	2

TABELA 2: Moda. Bolniki vključeni v analizo po stadiju bolezni in obdobju opazovanja.

TABLE 2: Testis. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage							
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%	%	%	
Moški Males	1983–87 204	102	50,0	58	28,4	42	20,6	2	1,0
	1988–92 247	117	47,4	95	38,5	35	14,2	0	0,0
	1993–97 333	161	48,3	124	37,2	45	13,5	3	0,9

TABELA 3: Moda. Opazovano in relativno petletno preživetje po obdobju opazovanja s 95 % intervalom zaupanja (IZ).

TABLE 3: Testis. Observed and relative five-year survival by period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano / Observed (%)					
	Moški / Males					
	Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	89	(85-93)	82	(77-85)	81	(75-87)
1988-92	94	(91-97)	89	(85-93)	87	(83-91)
1993-97	97	(95-99)	94	(91-97)	93	(90-96)

Obdobje/ Period	Relativno / Relative (%)					
	Moški / Males					
	Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	90	(86-94)	83	(78-88)	83	(77-89)
1988-92	95	(92-98)	90	(86-94)	90	(85-95)
1993-97	97	(95-99)	96	(93-99)	96	(93-99)

v SB v Novem mestu, v 5 % v SB v Murski Soboti, v 4,5 % v SB v Šempetru pri Novi Gorici, v 2,5 % v SB v Izoli, v 1 % v SB na Jesenicah. Na Onkološkem inštitutu v Ljubljani sta pričela prvo zdravljenje 2 % bolnikov.

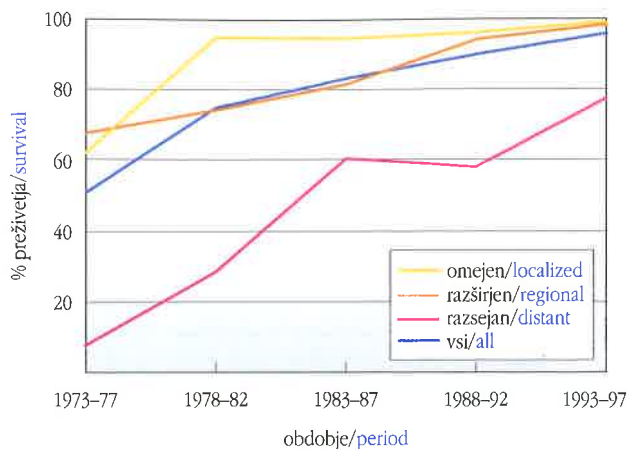
V letih 1993-97 je bilo relativno petletno preživetje za 13 % večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo pri bolnikih z razširjeno in razsejano boleznijo, z razširjeno v obdobju 1988-92, z razsejano pa v obdobju 1993-97. Preživetje je bilo pri bolnikih do 45. leta starosti praktično enako kot pri tistih starih 45 do 54 let (slika 3), pri bolnikih s seminomi pa večje kot pri bolnikih z ostalimi malignomi kličnih celic (slika 4).

Izsledki študije EUROCARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje za raka moda 86,8 % (85,4-88,3), v Sloveniji 89,8 % (86,6-93,1). Največje preživetje je bilo 94,3 % na Norveškem.

Marjeta Stanovnik, Onkološki inštitut Ljubljana

Preživetje bolnikov z omejeno boleznijo je bilo v vseh letih opazovanja zelo veliko in se ni bistveno povečevalo. Tudi način zdravljenja teh bolnikov se ni mnogo spreminjal. Večja sprememba v načinu zdravljenja bolnikov s seminomi je bila leta 1992. Do tega leta smo vsem bolnikom z omejenim seminomom po orhidektomiji dodatno obsevali regionalne bezgavke. Obsevanje je bilo dolgotrajno in bolnike iz oddaljenih krajev smo morali hospitalizirati. Študije pa so pokazale, da je bilo preživetje in število relapsov pri obsevanih bolnikih in pri tistih z dopolnilno kemoterapijo s karboplatinom enako. Zato smo po letu 1992 kot dopolnilno zdravljenje pri teh bolnikih uvedli karboplatin. Zdravljenje je bistveno krajše, lahko se izvaja ambulantno in stranski toksični učinki so minimalni (1).

Pri razširjeni in razsejani bolezni se je preživetje začelo večati po letu 1978, ko smo v zdravljenje uvedli cisplatin. Kombiniranje z novimi učinkovitimi citostatiki (etopozid, ifosfamid) je prav tako pripomoglo k večjemu preživetju. Tudi napredek



SLIKA 2: Relativno petletno preživetje bolnikov z rakom moda, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

FIGURE 2: Relative five-year survival of testicular cancer patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

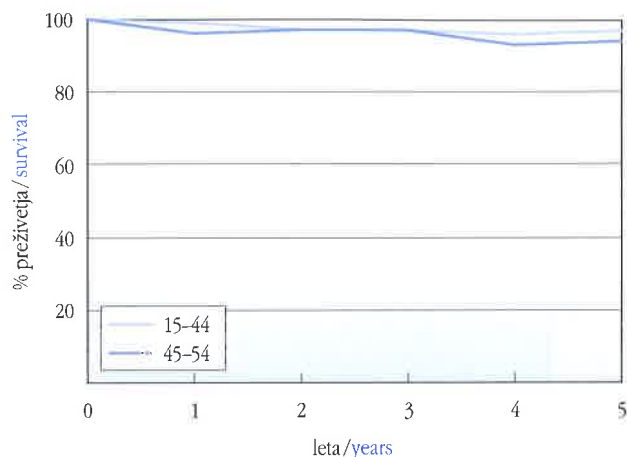
In the period 1993-97, 99% of patients underwent specific treatment. Surgery in combination with chemotherapy was applied as primary treatment in 63% of patients, 21% of patients underwent surgery alone, 15% of patients received surgery and radiotherapy, and 1% surgery, chemo-, and radiotherapy. Primary treatment was started at the Department of Urology, UMC in Ljubljana in 53% of patients, in the General Hospitals in Maribor and Celje in 9% of patients, in 7% in the General Hospital in Slovenj Gradec, in 6% in the General Hospital in Novo mesto, in 5% in the General Hospital in Murska Sobota, in 4.5% the General Hospital in Šempeter pri Novi Gorici, in 2.5% in the General Hospital in Izola, in 1% in the General Hospital in Jesenice. At the Institute of Oncology, primary treatment was started in 2% of testicular cancer patients.

The relative five-year survival rate of the patients was 13% higher in the years 1993-97 than in the years 1983-87 (Table 1). The survival improved in the patients with regional and metastatic diseases, in the respective periods 1988-92 and 1993-97. The survival of the patients below the age of 45 years was practically the same as of the patients in the age group of 45-54 years (Figure 3). The survival of patients with seminoma was higher than that of patients with other germ cell malignancies (Figure 4).

According to the EUROCARE-3 study results for the period 1990-94 in Europe, the age-standardized relative survival rate of the patients with testicular cancer was 86.8% (85.4-88.3), while in Slovenia, it was 89.8% (86.6-93.1). The highest rate of 94.3% was recorded in Norway.

Marjeta Stanovnik, Institute of Oncology Ljubljana

The survival of patients with localized disease was high throughout the observation period and was not significantly increasing. The treatment modalities for these patients did not change much, except in 1992 in the treatment of patients with seminoma. Until then, all patients with localized seminoma



SLIKA 3: Relativno petletno preživetje bolnikov z rakom mod, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of testicular cancer patients diagnosed in the period 1993–1997 by age.

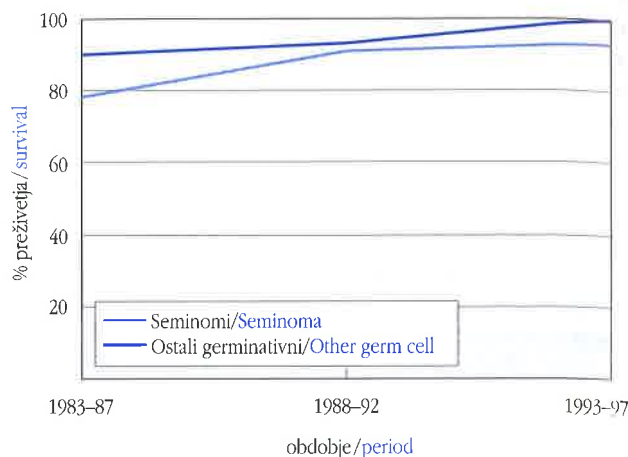
v operativni tehniki je doprinesel k večji učinkovitosti posegov in k zmanjšanju pooperativnih zapletov. Za preprečevanje zapletov po intenzivni kemoterapiji smo po letu 1993 pričeli uporabljati rastne faktorje, kar je pripomoglo k boljšim rezultatom zdravljenja.

Večji odstotek mikroskopsko potrjenih primerov je omogočil večjemu številu bolnikov najbolj ustrezen način zdravljenja. Za večje preživetje je bila pomembna tudi koncentracija bolnikov v dveh centrih (Onkološki inštitut ali Klinični oddelek za urologijo KC), kjer se je nadaljevalo primarno zdravljenje, ne glede na to, kje v Sloveniji je bilo pričeto.

Čeprav je delež bolnikov z omejeno boleznijo večji, jih je še vedno preveč odkritih v razširjeno ali razsejano boleznijo. Očitno se diagnostične metode v zadnjih letih niso bistveno izboljšale, pa tudi ozaveščenost moških ni večja. Potrebno bo vložiti še več truda v izobrazbo zdravnikov in mladostnikov.

VIR

1. Bosl GJ, Bajorin DF, Scheinfeld J, Motzer RJ, Chaganti RSK. Cancer of the testis. In: deVita VTJr, Hellman S, Rosenberg SA, eds. Cancer: principles and practice of oncology. 6th ed. Philadelphia: Lippincott, 2001: 1491–518.



SLIKA 4: Relativno petletno preživetje bolnikov z rakom mod, zbolelih v letih 1983–1997 po obdobjih diagnoze in histološki vrsti.

FIGURE 4: Relative five-year survival of testicular cancer patients diagnosed in the period 1983–1997 by period of diagnosis and histology.

underwent orchidectomy and received postoperative irradiation to regional lymph nodes. As radiotherapy usually lasted long, the patients from other regions had to be hospitalized. The end-results of studies that compared the survivals of and relapses in the patients treated by radiotherapy or by adjuvant chemotherapy with carboplatin were practically the same. And for that reason, these patients are receiving the adjuvant chemotherapy with carboplatin from 1992 onwards. This therapy is less time-consuming. It can be performed also in out-patient departments and has minimal toxic effects (1).

The survival of patients with regional and metastatic disease started to grow up after the year 1978 when the therapy with cisplatin was introduced. The combinations of new cytostatics (etoposide and ifosfamide) as well as some improvements in surgical techniques that reduced considerably postoperative complications had a favorable effect on survival. In the prevention of postchemotherapeutic complications, we have been using growth factors since 1993, which improved considerably the treatment results.

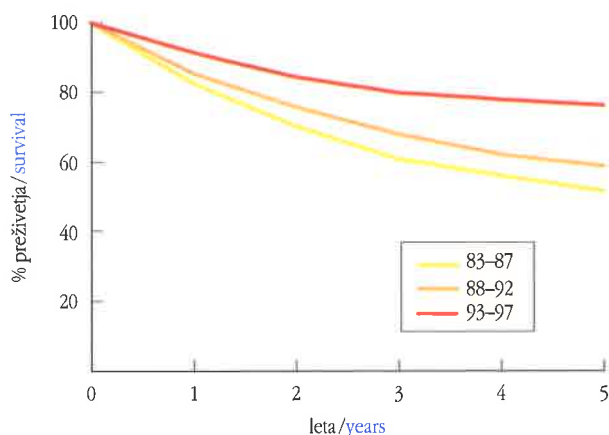
A higher percentage of microscopically confirmed cases enabled that more patients received the most properly selected treatment modality. Another factor that had a positive effect on survival was the concentration of testicular cancer patients in two health centers, *viz.* Institute of Oncology in Ljubljana and Department of Urology, UMC, Ljubljana. All the patients were referred to these two centers for further treatment, irrespective of the fact that they had received primary therapy in any other health institution in Slovenia.

Though the percentage of patients with localized disease has been observed to be higher, the patients with advanced disease are nevertheless too many. Evidently, no progress has been made in recent years in the field of diagnostics, neither any attempt to increase the awareness of men of the risks of this cancer. In the future, more efforts should be put into special training of physicians and educating the youngsters.

MALIGNI MELANOM

MALIGNANT MELANOMA

MKB 8 / ICD 8: 172



SLIKA 1: Relativno petletno preživetje bolnikov z malignim melanomom, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of malignant melanoma patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolel za malignim melanomom 901 moški in 1144 žensk, od tega v letih 1993–97 423 moških in 487 žensk. V analizo ni bilo vključenih 74 (2%) bolnikov.

V opazovanem 15-letnem obdobju se je incidenca maligne melanoma večala. V letih 1983–87 je bila groba incidenčna stopnja 4,5/100.000 moških in 5,8/100.000 žensk, v letih 1993–97 pa 8,8/100.000 moških in 9,6/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal z 98% v letih 1983–87 na 100% v letih 1993–97.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila. V zadnjem obdobju je bil največji delež bolnikov ob diagnozi mlajši od 45 let (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila. V letih 1993–97 je bilo odkrite več bolezni v omejenem in razširjenem in manj v razsejanem stadiju bolezni (tabela 2). Povprečna debelina tumorja se je manjšala (1).

V letih 1993–97 je bilo specifično zdravljenih 98% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (63%) samo kirurško, v 32% pa kombinacija operacije in imunoterapije; z ostalimi kombinacijami je bilo zdravljenih 5% bolnikov. V 20% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 19% na Kliničnem oddelku za plastično kirurgijo in opeklino KC v Ljubljani, v 10% na Kliničnem oddelku za dermatovenerologijo KC, v 20% v SB v Mariboru, v 7% v Celju, po 4% v Šempetru pri Novi Gorici in Novem mestu, po 3%

TABELA 1: Maligni melanom. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Malignant melanoma. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški Males	1983-87	198	0	46	45	56	32	19
	1988-92	266	0	66	56	64	48	32
	1993-97	424	0	117	82	95	86	44
Ženske Females	1983-87	273	1	91	41	44	56	40
	1988-92	357	1	111	68	80	55	42
	1993-97	480	0	122	110	95	89	64

In the period 1983–97, a total of 901 male and 1,144 female patients were diagnosed with malignant melanoma; of these, 432 males and 487 females were diagnosed with this cancer in the period 1993–97. Seventy-four patients (2%) were not included in the analysis.

In the observed 15-year period, the incidence of malignant melanoma was increasing. In 1983–87, the crude incidence rate was 4.5/100,000 in males and 5.8/100,000 in females, whereas in 1993–97, it was 8.8/100,000 in males and 9.6/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 2%, i. e. from 98% to 100%.

The age distribution of patients included into the analysis has changed. In the last observation period, a higher number of patients aged less than 45 years was detected at diagnosis (Table 1). The stage distribution at diagnosis changed, too. In the last observation period 1993–97, a higher percentage of patients with localized and regional disease and a lower percentage of patients with metastatic disease were observed (Table 2). A slight decrease of the mean thickness of the tumor was noted (1).

In the period 1993–97, 98% of patients underwent specific treatment. Surgery alone was applied as primary treatment in 63% of patients, 32% of patients were treated with a combination of surgery and immunotherapy, and 5% were treated with other combinations. Primary treatment was started at the

TABELA 2: Maligni melanom. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

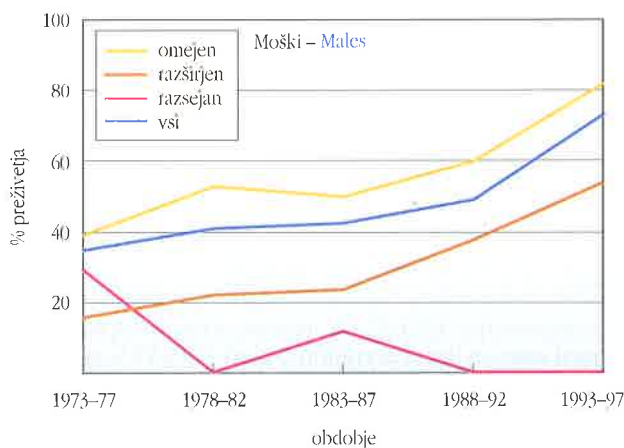
TABLE 2: Malignant melanoma. Patients included in the analysis by sex, stage and period of observation.

	Obdobje/ Period	Skupaj/ All	Stadij / Stage							
			Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%	%		
Moški Males	1983-87	198	142	71,7	26	13,1	19	9,6	11	5,6
	1988-92	266	184	69,2	49	18,4	23	8,6	10	3,8
	1993-97	424	314	74,1	76	17,9	19	4,5	15	3,5
Ženske Females	1983-87	273	212	77,7	29	10,6	20	7,3	12	4,4
	1988-92	357	274	76,8	56	15,7	18	5,0	9	2,5
	1993-97	480	389	81,0	59	12,3	14	2,9	18	3,8

TABELA 3: Malignni melanom. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Malignant melanoma. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	77	(71-83)	47	(40-54)	36	(29-43)	84	(79-89)	63	(57-69)	53	(47-59)
1988-92	76	(71-81)	54	(48-60)	42	(36-48)	90	(87-93)	71	(66-76)	61	(56-66)
1993-97	89	(86-92)	71	(67-75)	63	(58-68)	91	(88-94)	77	(73-81)	71	(67-75)

Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	79	(73-85)	51	(43-59)	42	(34-50)	85	(80-90)	67	(57-69)	60	(53-67)
1988-92	78	(73-83)	59	(52-66)	49	(42-56)	91	(88-94)	75	(66-76)	67	(61-73)
1993-97	91	(88-94)	77	(72-82)	73	(67-79)	93	(90-96)	82	(73-81)	79	(74-84)



SLIKA 2: Relativno petletno preživetje bolnikov z malignim melanomom, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

v Slovenj Gradcu in v Murski Soboti, v 2,5% v zasebnih ordinacijah, po 2% v Izoli in na Kliničnem oddelku za splošno kirurgijo KC, v 1% na Jesenicah. Posamezne bolnike so operirali še na drugih kliničnih oddelkih KC ter v bolnišnicah Trbovlje, Ptuj in Brežice.

V letih 1993-97 je bilo relativno petletno preživetje za 24% večje kot v letih 1983-87 (slika 1). Preživetje se je povečalo pri bolnikih z omejeno in razširjeno boleznijo, bolj pri moških kot pri ženskah. Glede na starost je bilo pri ženskah preživetje večje pri mlajših od 65 let. Pri moških pa je bilo preživetje večje pri mlajših od 55 let. V starosti 65-74 let je bilo opazovano preživetje enako tistemu v starosti 55-64 let, relativno pa je bilo zaradi načina izračunavanja večje (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje pri bolnikih z malignim melanomom pri moških 74,7% (72,9-76,6) in pri ženskah 84,4% (83,2-85,5), v Sloveniji pa pri moških 60,6% (53,9-68,1) in pri ženskah 70,1% (64,6-76,1). Največje preživetje pri moških je bilo 87,3% na Tirolskem v Avstriji in pri ženskah 91,7% na Islandiji.

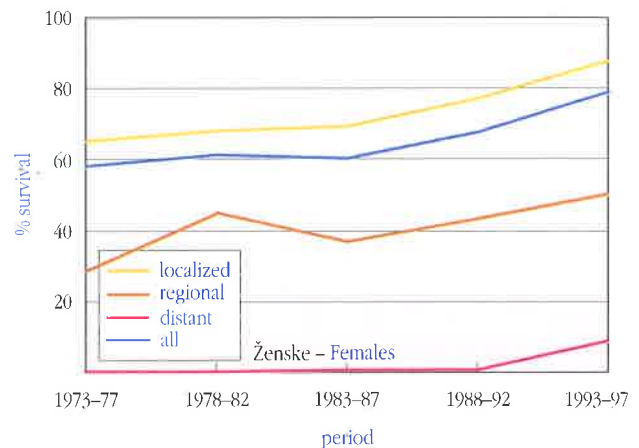
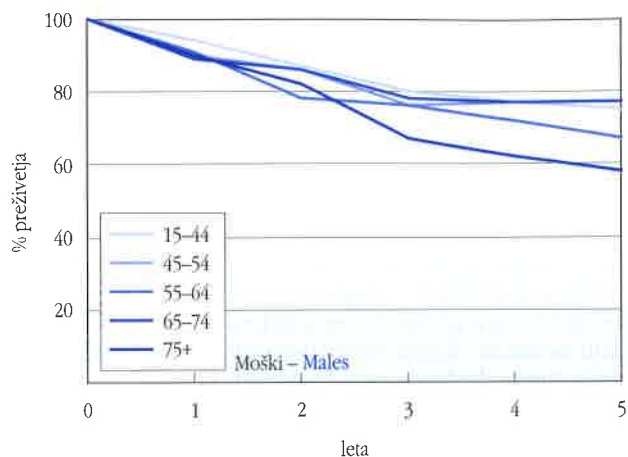


FIGURE 2: Relative five-year survival of malignant melanoma patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

Institute of Oncology Ljubljana in 20% of patients, in 19% at the Department of Plastic Surgery and Burns, UMC in Ljubljana, in 10% at the Department Dermatovenereology, UMC, Ljubljana, in 20% in the General Hospital in Maribor, in 7% in the General Hospital in Celje, in 4% in the General Hospitals Šempeter pri Novi Gorici and Novo Mesto, in 3% in each of General Hospitals in Slovenj Gradec and in Murska Sobota, in 2,5% at private clinics, in 2% in each of the following institutions, the General Hospital in Izola and at the Department of General Surgery, UMC in Ljubljana, and in 1% in the General Hospital in Jesenice. A few individual patients were operated on at other departments of UMC in Ljubljana and the General Hospitals in Trbovlje, Ptuj and Brežice.

The relative five-year survival rate was 24% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The survival improved in the patients with localized and regional disease. The increase was higher in men than in women. The comparison by age shows that the survival was higher in women aged less than 65 years and in men younger than 55 years. In the age group of 65-74 years, the observed survival was the



SLIKA 3: Relativno petletno preživetje bolnikov z malignim melanomom, zbolelih v letih 1993–1997 po starosti.

Marko Hočevar, Onkološki inštitut Ljubljana

Preživetje bolnikov z malignim melanomom je tako kot pri drugih vrstah raka odvisno predvsem od stadija bolezni ob začetku zdravljenja in od načina zdravljenja.

Stadij bolezni ob začetku zdravljenja je pri malignem melanomu v največji meri odvisen od ozaveščenosti prebivalstva. Diagnoza zgodnjih oblik lokaliziranega malignega melanoma je v večini primerov možna že samo z natančno inspekcijo, ki se je lahko ob ustrezni kampanji hitro in uspešno nauče tudi laiki. Tako ima Avstralija, ki je država z najvišjo incidenco melanoma na svetu, najboljše preživetje bolnikov z malignim melanomom. Z doslednim upoštevanjem enostavnega ABCDE sistema diagnosticiranja kožnega malignega melanoma pri samopregledovanju prebivalstva so dosegli, da je povprečna debelina melanomov nižja od 1 mm. Temu zgledu uspešno sledijo tudi države z nizko incidenco malignega melanoma kot so Anglija in Švedska.

V načinu zdravljenja bolnikov z malignim melanomom je prišlo v zadnjem desetletju do sprememb, ki bodo najverjetneje dodatno izboljšale preživetje nekaterih podskupin bolnikov. Tako smo dobili biopsijo varovalne bezgavke, ki nam omogoča bistveno natančnejšo določitev stadija bolezni ob postavitvi diagnoze. To nam omogoči, da pričnemo zdraviti bolnike z regionalnimi metastazami (stadij III) že v fazi mikrometastaz, s čimer izboljšamo prognozo te podskupine za približno 25% (1, 2).

Omogoči nam tudi homogene skupine bolnikov za različne načine adjuvantnega zdravljenja. Pred obdobjem biopsije varovalne bezgavke so bile skupine bolnikov v različnih študijah adjuvantnega zdravljenja preveč heterogene (pomešani so bili bolniki z mikrometastazami in tisti brez njih), da bi lahko dokazali uspešnost nekaterih načinov adjuvantnega zdravljenja (imunoterapija, kemoimunoterapija).

Tudi v Sloveniji imamo relativno 5 letno preživetje za 24% večje v obdobju 1993–97 v primerjavi z obdobjem v letih 1983–87. To lahko pripišemo večji ozaveščenosti prebivalstva. V obdobju 1993–97 je bil odstotek bolnikov v omejenem in razširjenem stadiju večji, manjši v razsejanem stadiju pa tudi povprečna debelina tumorja je bila manjša (1).

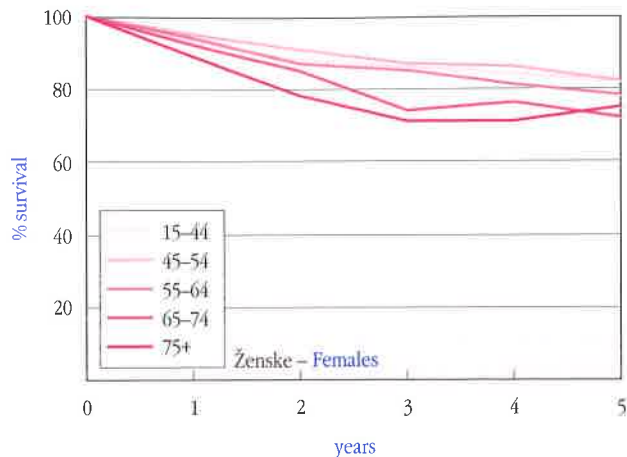


FIGURE 3: Relative five-year survival of malignant melanoma patients diagnosed in the period 1993–1997 by age.

same as in the age group of 55–64 years, whereas the relative survival was slightly higher (Figure 3).

According to the EURO-CARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with malignant melanoma was 74.7% (72.9–76.6) in male patients and in female patients 84.4% (83.2–85.5), while in Slovenia, it was 60.6% (53.9–68.1) in male patients and 70.1% (64.6–76.1) in female patients. The highest rates of 87.3% in male and of 91.7% in female patients were observed in Tyrol in Austria and Iceland, respectively.

Marko Hočevar, Institute of Oncology Ljubljana

The survival of patients with malignant melanoma depends upon the stage of disease at the beginning of the therapy and upon the selected treatment modality. The stage of the disease at the beginning of the therapy depends to a large degree on the awareness of the population of the risks of this disease. With a meticulous examination that can be successfully learned also by people who are not medical experts it is possible to diagnose a localized malignant melanoma in its early stage. Australia, a country with the highest incidence of malignant melanoma in the world, is known to have the best survival of these patients in the world. Following the recommendations of the ABCDE system for diagnosing malignant melanoma by self-inspection, the mean thickness of the detected melanomas was less than 1 mm. The same system was adopted also by the countries with low malignant melanoma incidence, such as England and Sweden.

In the most recent decade, some progress was made in the treatment of malignant melanoma that will additionally improve the survival at least in some of the subgroups of malignant melanoma patients. One of these advances is sentinel node biopsy, a method that allows an accurate determination of the disease stage at diagnosis. We can therefore start to treat the patients with regional metastases (stage III) already in the phase of micrometastases, thereby improving the prognosis of this subgroup of patients by 25% (1, 2). The disease staging at diagnosis is most helpful also in gathering the patients into more homogenous treatment groups receiving different

V obdobju 1993–97 so bili bolniki z razširjeno boleznijo v večini primerov deležni standardnega kirurškega zdravljenja – terapevtske limfadenektomije v za to usposobljenem centru (Onkološki inštitut). Tudi to se kaže v izboljššanem preživetju te podskupine bolnikov.

V obdobju 1993–1997 je največji delež bolnikov že mlajši od 45 let. Starost bolnikov z malignim melanomom pa predstavlja enega od pomembnejših prognostičnih dejavnikov. Starejši bolniki imajo slabšo prognozo.

Ob nadaljnji večji ozaveščenosti prebivalstva (mesečno samopregledovanje, zaščita pred delovanjem UV žarkov) ter ob doslednem upoštevanju priporočil zdravljenja (biopsija varovalne bezgavke, adjuvantna radioterapija, priključitev v mednarodne študije adjuvantnega zdravljenja – PegIntron) lahko upamo, da bo postalo preživetje bolnikov z malignim melanomom v Sloveniji primerljivo z ostalo Evropo in razvitim svetom.

Zvonimir Rudolf, Onkološki inštitut Ljubljana

Relativno preživetje bolnikov z malignim melanomom se je v obdobju 1993–97 povečalo v primerjavi z leti 1983–87. Izboljšanje preživetja lahko pripišemo boljši zdravstveni prosvetljenosti prebivalstva in deloma učinkovitejšemu zdravljenju.

Prognoza bolnikov je odvisna od debeline primarnega tumorja in ulceracije, v področno razširjenem stadiju pa od števila prizadetih bezgavk. Povprečna debelina tumorjev je bila v Sloveniji v letih 1993–97 manjša kot v preteklih obdobjih (1), več bolnikov je bilo odkritih v omejenem in področno razširjenem stadiju in manj z razsejano boleznijo.

Na Onkološkem inštitutu uspešno deluje multidisciplinarni tim za melanom in bolniki iz vse Slovenije se usmerjajo v melanomsko ambulanto.

Metoda izbora za zdravljenje primarnega malignega melanoma je slejkoprej radikalna odstranitev primarnega tumorja, pri razsoju v področne bezgavčne lože pa disekcija bezgavk. Sicer ni bistvenih premikov na področju sistemskega zdravljenja, adjuvantno zdravljenje z interferonom je še vedno v fazi preizkušanja, predvsem s srednjimi odmerki interferona.

V doktrini zdravljenja kot tudi v klasifikaciji melanoma je prišlo do sprememb šele v zadnjih dveh letih. Uvaja se biopsija varovalne bezgavke in nov sistem klasifikacije, ki bosta imela pomen šele v prihodnosti.

VIRI

1. Pihl A. Trend incidence in preživetja bolnikov s kožnim malignim melanomom v Sloveniji v obdobju 1980–1999 glede na izbrane napovedne dejavnike preživetja. Magistrska naloga. Ljubljana: Medicinska fakulteta, 2003.
2. Balch CM, Bultrazvokaid AC, Soong SJ et al. Final version of the American Joint Committee on cancer staging system for cutaneous melanoma. *J Clin Oncol* 2001; 19: 3635–48.
3. Balch CM, Soong SJ, Gershenwald JE et al. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on cancer melanoma staging system. *J Clin Oncol*. 2001; 19: 3622–34.

adjuvant therapies. Before the initiation of the sentinel node biopsy the treatment groups of patients included into the studies on adjuvant therapies were too heterogeneous (consisting of the patients with metastases and those without them) to prove the effectiveness of the adjuvant therapy dealt with in a study, *viz.* of immunotherapy or chemoimmunotherapy.

Comparing the observation periods 1983–78 and 1993–97, an increase of 24% was observed in the relative five-year survival in Slovenia. This is attributable to a heightened awareness of the population of the risks related to this disease. In the observation period 1993–97, a higher percentage of the patients with localized and regional disease and lower percentage of those with metastatic disease were observed (Table 2). Besides, the mean tumor thickness also decreased (1).

In the period 1993–97, the majority of melanoma patients with regional disease received standard surgical treatment, *i. e.* therapeutic lymphadenectomy carried out at the Institute of Oncology, at a cancer center that is specialized for such interventions. This very fact also contributed to the improvement of the survival of this subgroup of patients.

In the period 1993–97, the majority of melanoma patients was younger than 45 years, which is of vital importance since the age of malignant melanoma patients is one of the important prognostic factors. Elderly patients have poorer prognosis

With further rise of the awareness of people by recommending them self-inspection and protection against UV radiation and with strict observing the treatment guidelines, *e. g.* sentinel node biopsy, adjuvant radiotherapy and joining the international study on adjuvant therapy – PegIntron, we may expect that the survival of patients with malignant melanoma in Slovenia will become comparable with that in Europe and of the rest of the developed world.

Zvonimir Rudolf, Institute of Oncology Ljubljana

In the observation period 1993–97, the relative survival of the malignant melanoma patients was better than in the period 1983–87. This improvement may be due to a higher awareness of the population of the risks of the disease as much as to a more effective treatment. The prognosis depends mainly on the thickness of the primary tumor and on ulceration, whereas in regionally advanced disease, on the lymph node involvement. A larger decrease in the mean tumor thickness was observed in this period than in the earlier ones (1). In the last observation period, more patients with localized and regionally advanced disease and less patients with metastatic disease were detected than in earlier periods.

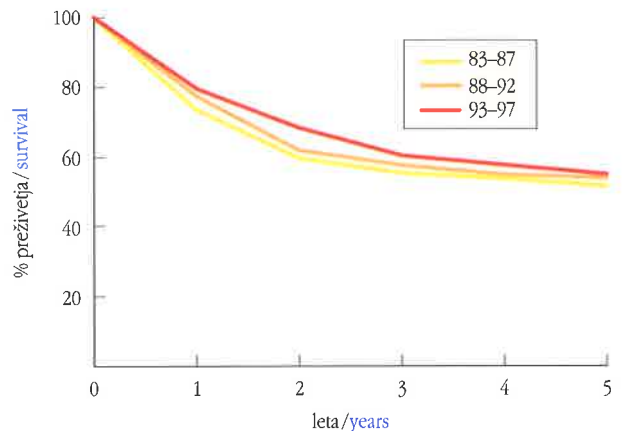
At the Institute of Oncology, a Multidisciplinary Advisory Team for Melanoma has been working successfully. Melanoma patients from all Slovenian regions are referred to this team.

The treatment of choice for primary malignant melanoma is by and large radical excision of primary tumor and dissection of the lymph nodes in case of metastatic spread into regional lymph nodes. In systemic treatment of malignant melanoma, no major changes have been made, while adjuvant therapy with interferon is still under study, in particular the therapy with medium doses of interferon.

In the treatment guidelines as well as in classification, some progress has been observed only in the recent two years. Important innovations are sentinel node biopsy and new classification system. Their impact will be recognized only in the future.

SARKOMI MEHKIH TKIV

SOFT TISSUE SARCOMAS



SLIKA 1: Relativno petletno preživetje bolnikov s sarkomi mehkih tkiv, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of soft tissue sarcoma patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za sarkomi mehkih tkiv 383 moških in 473 žensk, od tega v letih 1993–97 146 moških in 184 žensk. V celotnem obdobju je bilo 49% sarkomov v notranjih organih, 11% v retroperitoneju in 40% na drugih lokacijah. V analizo ni bilo vključenih 14 (2%) bolnikov, ker je bil pri njih sarkom ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca sarkomov večala. V letih 1983–87 je bila groba incidenčna stopnja 2,5/100.000 moških in 2,9/100.000 žensk, v letih 1993–97 pa 3/100.000 moških in 3,6/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnikov starejših od 55 let. Razširjenost bolezni ob diagnozi se je spremenila (tabela 2). V letih 1993–97 je bilo več bolnikov odkritih v omejenem stadiju bolezni.

V letih 1993–97 je bilo prvo zdravljenje v največjem odstotku kirurško (61%). Kemoterapija je bila dodana operaciji v 11%, obsevanje v 13%, kemoterapija in obsevanje skupaj pa v 7%. Samo z obsevanjem so zdravili 4% bolnikov, samo s kemoterapijo 1%, s kombinacijo obeh načinov pa 4%.

V letih 1993–97 je bilo relativno petletno preživetje pri moških za 9% večje kot v letih 1983–87, medtem ko se pri žen-

TABELA 1: Sarkomi mehkih tkiv. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Soft tissue sarcoma. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87	117	16	35	15	17	21	13
	1988-92	121	5	42	25	26	17	6
	1993-97	141	7	46	17	27	34	10
Ženske Females	1983-87	140	9	30	30	25	25	21
	1988-92	145	11	31	29	28	28	18
	1993-97	180	9	41	23	37	46	24

In the period 1983–97, a total of 383 male and 473 female patients were diagnosed with soft tissue sarcomas; of these, 146 males and 184 females were diagnosed with this cancer in the period 1993–97. In the entire observation period, 49% of all sarcomas developed in the visceral organs, 11% on the retroperitoneum and 40% on other sites. In 14 patients (2%), sarcoma was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of sarcomas was increasing. In 1983–87, the crude incidence rate was 2.5/100,000 in males and 2.9/100,000 in females, whereas in 1993–97, it was 3/100,000 in males and 3.6/100,000 in females.

The age distribution of patients included into the analysis changed (Table 1). In the period 1993–97, a higher percentage of patients over 55 years were included into the analysis. The stage distribution of the disease at diagnosis changed, too (Table 2). In the last observation period 1993–97, a higher percentage of patients with localized disease was observed.

In the period 1993–97, surgery alone was performed in 61% of patients, 11% of patients received postoperative chemotherapy, 13% received postoperative radiotherapy, and 7% both postoperative chemotherapy and radiotherapy. Radiotherapy

TABELA 2: Sarkomi mehkih tkiv. Bolniki vključeni v analizo po stadiju bolezni in obdobju opazovanja.

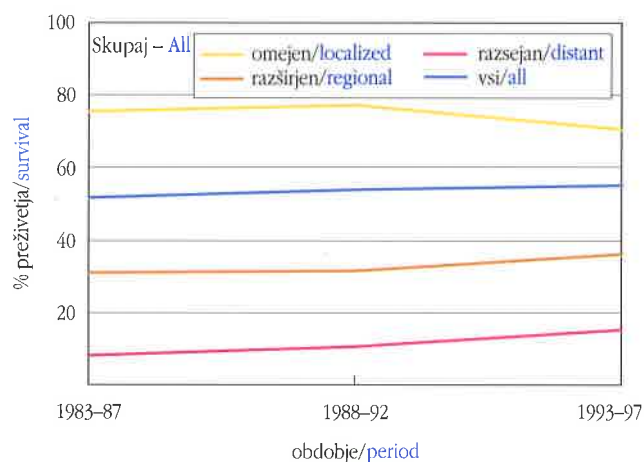
TABLE 2: Soft tissue sarcoma. Patients included in the analysis by stage and period of observation.

Obdobje/ Period	Skupaj/ All	Omejen/ Localized	Stadij/Stage							
			%	Razširjen/ Regional	%	Razsejan/ Distant	%	Neznan/ Unknown	%	
Skupaj All	1983-87	257	133	51,8	76	29,6	38	14,8	10	3,9
	1988-92	266	144	54,1	78	29,3	31	11,7	13	4,9
	1993-97	321	195	60,7	81	25,2	37	11,5	8	2,5

TABELA 3: Sarkomi mehkih tkiv. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Soft tissue sarcoma. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje / Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	68	(59-77)	49	(40-58)	42	(33-51)	75	(68-82)	54	(46-62)	49	(41-57)
1988-92	73	(65-81)	47	(38-56)	45	(36-54)	79	(72-86)	60	(52-68)	51	(43-59)
1993-97	78	(71-85)	57	(49-65)	51	(42-60)	78	(72-84)	55	(47-62)	48	(40-56)

Obdobje / Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ / CI	3	IZ / CI	5	IZ / CI	1	IZ / CI	3	IZ / CI	5	IZ / CI
1983-87	70	(61-79)	53	(43-63)	49	(38-60)	76	(69-83)	58	(49-67)	54	(45-63)
1988-92	74	(66-82)	50	(40-60)	50	(40-60)	80	(73-87)	63	(54-72)	57	(48-66)
1993-97	80	(73-87)	62	(53-71)	58	(48-68)	79	(73-85)	59	(51-67)	53	(45-61)

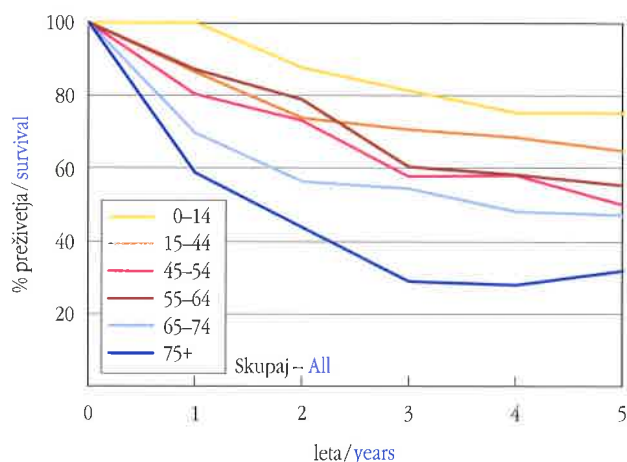


SLIKA 2: Relativno petletno preživetje bolnikov s sarkomi mehkih tkiv, zbolelih v letih 1973-1997 po stadiju in obdobju diagnoze.

FIGURE 2: Relative five-year survival of soft tissue sarcoma patients diagnosed in the period 1973-1997 by stage and period of diagnosis.

skah ni pomembno spremenilo (tabela 3). Tako se je relativno preživetje obeh spolov skupaj povečalo le za 4% (slika 1). Preživetje se je povečalo pri lokalno razširjeni in razsejani bolezni, pri omejeni pa se je nekoliko zmanjšalo (slika 2). Preživetje je bilo največje pri otrocih in mladih odraslih, najmanjše pa v starosti 65-74 let (slika 3).

V študiji EURO-CARE-3 so obravnavali le preživetje bolnikov s sarkomi glave, trupa in okončin. Izsledki kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje pri bolnikih s sarkomi mehkih tkiv pri moških 54% (51-57,1) in pri ženskah 55,6% (52,4-59), v Sloveniji pa pri moških 56,2% (42,1-75) in pri ženskah 62,5% (50,8-76,8). Največje preživetje pri moških je bilo 61,8 v treh okrožjih Francije (Bas-Rhin, Calvados in Cote d'Or) in pri ženskah 64,2% na Tirolskem v Avstriji.



SLIKA 3: Relativno petletno preživetje bolnikov s sarkomi mehkih tkiv, zbolelih v letih 1993-1997 po starosti.

FIGURE 3: Relative five-year survival of soft tissue sarcoma patients diagnosed in the period 1993-1997 by age.

alone was applied in 4% of patients, chemotherapy alone in 1% of patients, and a combination of both in 4% of patients.

The relative five-year survival rate of male patients was 9% higher in the years 1993-97 than in the years 1983-87, whereas in female patients, it did not change in that period (Table 3). The overall survival of both sexes thus increased only by 4% (Figure 1). The survival increased in the patients with regionally advanced disease and in those with metastatic disease. In the patients with localized disease, it slightly dropped (Figure 2), while it was the highest in children and young adults and the lowest in the patients aged between 65-74 years (Figure 3).

The EURO-CARE-3 study comprises only the data on the survival of patients with sarcomas on the head, trunk, and limbs. According to the study results for the period 1990-94 in Europe, the age-standardized relative survival rate of the patients with soft tissue sarcomas was 54% (51-57.1) in male

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V primerjavi z ostalimi evropskimi državami smo prav pri zdravljenju sarkomov mehkih tkiv med najbolj uspešnimi. Razlogi za to so: centralizirano zdravljenje, multidisciplinarni pristop, uspešna kirurgija s histološko kontrolo radikalnosti operacije, planirano prvo zdravljenje na konziliju in sodelovanje v mednarodnih raziskavah. Le redki bolniki ob planiranju kombiniranega zdravljenja niso predstavljeni na konziliju.

Verjetno pa bi rezultate lahko še izboljšali. V vsem petnajstletnem obdobju se je namreč celokupno relativno petletno preživetje le malo izboljšalo (slika 1). V zadnjem petletnem obdobju se je izboljšalo le pri razsejani bolezni (verjetno zaradi agresivnejšega zdravljenja z operacijo in citostatiki). Pri lokalizirani bolezni pa se je poslabšalo (verjetno zaradi nestrokovnega prvega zdravljenja) (slika 2). Kirurg se ne bi smel lotiti prvega zdravljenja brez podpore patologa, ki po standardih opredeli radikalnost operacije in podrobneje opredeli vrsto teh redkih malignomov. Ob nepravilnem prvem zdravljenju je verjetnost lokalnega recidiva in pljučnih metastaz velika. Relativno petletno preživetje pa je pri bolnikih z razsejano boleznijo, za katero danes še nimamo ustreznih zdravil, porazno (1).

VIR

1. Brennan MF, Alektiar KM, Maki RG. Soft tissue sarcoma. In: deVita VT, Jr, Hellman S, Rosenberg SA, editors. Cancer: principles and practice of oncology. Vol. 2. Philadelphia: Lippincott, 2001: 1841–91.

patients and in female patients 55.6% (52.4–59), while in Slovenia, it was 56.2% (42.1–75) in male patients and 62.5% (50.8–76.8) in female patients. The highest rates of 61.8% and of 64.2% were observed respectively in male patients in three regions in France: Bas-Rhin, Calvados and Cote d'Or and in female patients in Tyrol in Austria.

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The comparison with other European countries reveals that Slovenia with its soft tissue sarcoma treatment results ranks among the most successful countries. Such effectiveness stems from centralized and multidisciplinary treatment approach, successful surgical intervention with histologically controlled radicality, treatment plan made by the Multidisciplinary Advisory Team for Sarcomas and participation in international research studies. Very few patients underwent combined treatment that had not been planned by Multidisciplinary Advisory Team.

The treatment results could eventually be further improved. In the whole 15-year observation period, the overall relative five-year survival insignificantly increased (Figure 1). In the last five-year observation period, a considerable rise was observed only in the patients with metastatic disease, which is possibly due to more aggressive treatment modality, combining surgery and chemotherapy. In the patients with localized disease, the survival declined probably because of inadequate primary treatment (Figure 2). A surgeon should never start primary treatment without the support of a pathologist who assesses the radicality of operation according to the set standards and determines the type of this rather rare malignancy. After improper primary treatment, the development of local recurrence and lung metastases is very likely. The relative five-year survival rate of the patients with distant metastases, for which no proper drugs are available, is dramatically low (1).

KOSTNI SARKOMI

BONE SARCOMAS

MKB 8 / ICD 8: 170

V obdobju 1983–97 je zbolelo za kostnimi sarkomi 108 moških in 109 žensk, od tega v letih 1993–97 37 moških in 33 žensk. V analizo so bili vključeni vsi bolniki.

V opazovanem 15-letnem obdobju se incidenca kostnih sarkomov ni spremenila. V letih 1983–87 je bila groba incidenčna stopnja 0,9/100.000 moških in 0,7/100.000 žensk, v letih 1993–97 pa 0,8/100.000 moških in 0,6/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je le nekoliko spremenila (tabela 1). Razširjenost bolezni ob diagnozi se je spremenila pri osteosarkomih (tabela 2). V letih 1993–97 je bilo več bolnikov odkritih v začetnem stadiju (T1) bolezni.

V letih 1993–97 je bilo samo z operacijo zdravljenih 29% bolnikov, z operacijo in citostatiki 26%, samo s citostatiki 22%, s citostatiki in obsevanjem 7%, z operacijo, citostatiki in z obsevanjem 7%, z operacijo in z obsevanjem 6% in 2% samo z obsevanjem. V 52% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 23% na Pediatrični kliniki v Ljubljani, v 6% v Mariboru, v 4% na Kliniki za nevrokirurgijo. Po en bolnik je bil zdravljen na Kliniki za maksilofacialno kirurgijo in v Ortopedski bolnici Valdoitra.

Relativno petletno preživetje prikazujemo za vsako histološko vrsto kostnega sarkoma posebej, ker se načini zdravljenja

TABELA 1: Kostni sarkomi. Bolniki vključeni v analizo po histološki vrsti, starosti in obdobju opazovanja.

TABLE 1: Bone sarcoma. Patients included in the analysis by histological type, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Osteogeni sarkom	1988-92	24	6	9	3	4	1	1
Osteogenic sarcoma	1993-97	31	9	13	2	6	0	1
Ewingov sarkom	1988-92	7	2	5	0	0	0	0
Ewing sarcoma	1993-97	6	1	5	0	0	0	0
Hondrosarkom	1988-92	19	0	7	4	3	2	3
Hondrosarcoma	1993-97	17	1	3	5	7	1	0

In the period 1983–97, a total of 108 male and 109 female patients were diagnosed with bone sarcomas; of these, 37 males and 33 females were diagnosed with this cancer in the period 1993–97. All patients diagnosed with bone sarcoma were included in the analysis.

In the observed 15-year period, the incidence of bone sarcomas was steady. In 1983–87, the crude incidence rate was 0.9/100,000 in males and 0.7/100,000 in females, whereas in 1993–97, it was 0.8/100,000 in males and 0.6/100,000 in females.

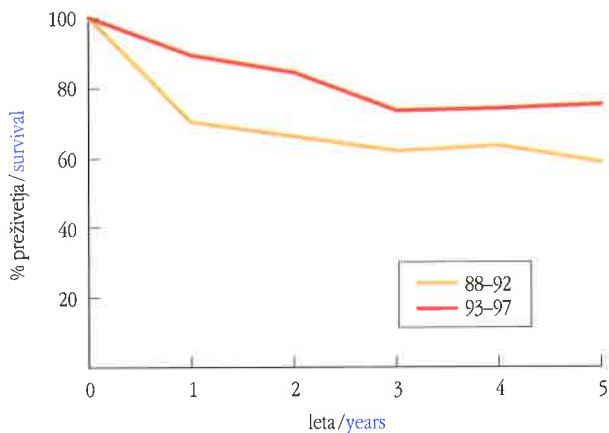
The age distribution of patients included into the analysis slightly changed (Table 1). The stage distribution of the disease at diagnosis changed, too. In the last observation period 1993–97, a higher percentage of patients with localized disease (T1) was observed.

In the period 1993–97, surgery alone was performed in 29% of patients, 26% were treated with surgery and postoperative chemotherapy, 22% of patients received chemotherapy alone, 7% were treated with surgery, postoperative chemotherapy and radiotherapy, 7% received chemotherapy and radiotherapy, 6% surgery and radiotherapy, and 2% radiotherapy alone. Primary treatment was started at the Institute of Oncology Ljubljana in 52% of patients, in 23% at the Department of

TABELA 2: Kostni sarkomi. Bolniki vključeni v analizo po stadiju bolezni in obdobju opazovanja.

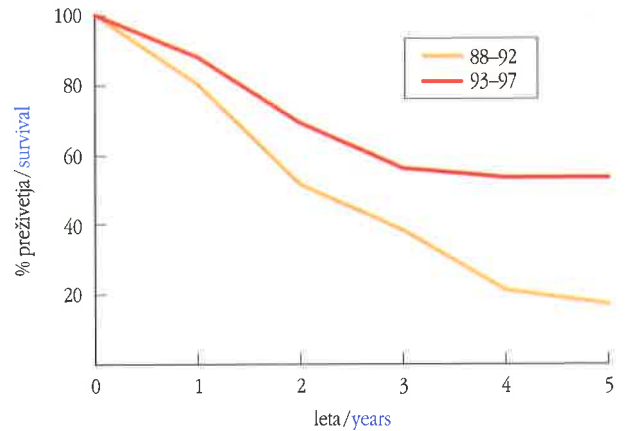
TABLE 2: Bone sarcoma. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized %	Razširjen/ Regional %	Razsejan/ Distant %	Neznan/ Unknown %					
Osteogeni sarkom	1988-92	24	3	12,5	18	75,0	3	12,5	0	0,0
Osteogenic sarcoma	1993-97	31	11	35,5	15	48,4	5	16,1	0	0,0
Ewingov sarkom	1988-92	7	2	6,5	2	28,6	3	42,9	0	0,0
Ewing sarcoma	1993-97	6	0	0,0	4	66,7	2	33,3	0	0,0
Hondrosarkom	1988-92	19	5	26,3	14	73,7	0	0,0	0	0,0
Hondrosarcoma	1993-97	17	4	23,5	11	64,7	1	5,9	1	0,0



SLIKA 1a: Relativno petletno preživetje bolnikov s hondrosarkomom, zbolelih v letih 1988–1997 po obdobju diagnoze.

FIGURE 1a: Relative five-year survival of hondrosarcoma patients diagnosed in the period 1988–1997 by period of diagnosis.



SLIKA 1b: Relativno petletno preživetje bolnikov z osteogenim sarkomom, zbolelih v letih 1988–1997 po obdobju diagnoze.

FIGURE 1b: Relative five-year survival of osteogenic sarcoma patients diagnosed in the period 1988–1997 by period of diagnosis.

TABELA 3: Kostni sarkomi. Opazovano in relativno petletno preživetje po obdobju opazovanja s 95% intervalom zaupanja (IZ).

TABLE 3: Bone sarcoma. Observed and relative five-year survival by period of observation with 95% confidence interval (CI).

Obdobje/Period	Opazovano/Observed (%)																	
	Osteogeni sarkom/Osteogenic sarcoma						Ewingov sarkom/Ewing sarcoma					Hondrosarkom/Hondrosarcoma						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1988–92	79	(62–96)	38	(18–58)	17	(2–32)	100	(–)	57	(20–94)	43	(6–80)	68	(47–89)	58	(35–81)	53	(20–76)
1993–97	87	(65–99)	55	(37–73)	52	(34–70)	100	(–)	17	(0–34)	17	(0–34)	88	(76–100)	71	(49–93)	71	(49–93)

Obdobje/Period	Relativno/Relative (%)																	
	Osteogeni sarkom/Osteogenic sarcoma						Ewingov sarkom/Ewing sarcoma					Hondrosarkom/Hondrosarcoma						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1988–92	80	(63–97)	38	(18–58)	17	(1–33)	100	(–)	57	(20–94)	43	(6–80)	70	(48–92)	62	(38–66)	58	(33–83)
1993–97	88	(66–100)	56	(38–74)	53	(34–72)	100	(–)	17	(0–34)	17	(0–34)	89	(78–100)	73	(50–96)	75	(51–99)

glede na histološko vrsto močno razlikujejo. Pri osteogenih sarkomih je bilo v letih 1993–97 relativno petletno preživetje za 36% večje kot v letih 1988–92, pri hondrosarkomu pa se je povečalo za 17% (slika 1a in b).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje odraslih bolnikov s kostnimi sarkomi pri moških 50,3% (45,6–55,5) in pri ženskah 55,4% (50,7–60,5), v Sloveniji pa pri ženskah 61,4% (44,4–85), za moške izračun starostne standardizacije ni bil možen (relativno petletno preživetje je bilo 33%). Največje preživetje pri moških je bilo 60,5% na Švedskem in pri ženskah 69,8% na Norveškem.

Branko Zakotnik, Onkološki inštitut Ljubljana

Po zgoraj navedenih podatkih, lahko zaključimo, da so sarkomi kosti: hondrosarkom, osteogeni sarkom in Ewingov sarkom redki tumorji in da se razen hondrosarkoma pojavljajo pri mlajših.

Paediatrics, UMC Ljubljana, in 6% in the General Hospital in Maribor, in 4% at the Department of Neurosurgery, UMC Ljubljana, and in 1% in each of the following institutions, the Department of Maxillofacial and Oral Surgery, UMC, Ljubljana and Orthopaedic Hospital in Valdoltra.

The relative five-year survival rates are given for each histology type separately because each particular type requires a different treatment modality. In the period 1993–97, the relative five-year survival rate of patients with osteogenic sarcomas was 36% higher than in the period 1988–92, in patients with Ewing's sarcoma, it decreased and increased in the patients with chondrosarcoma by 17% (Figures 1a, b and c).

According to the study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with bone sarcomas was 50.3% (45.6–55.5) in male patients and in female patients 55.4% (50.7–60.5), while in Slovenia, it was 61.4% (44.4–85) in female patients (for male patients the calculation was not possible). The highest rates of 60.5% and of 69.8% were observed in male and female patients in Sweden and Norway respectively.

HONDROSARKOM

Pojavlja se v vseh starostih. Edini način zdravljenja, ki zagotavlja ozdravitev, je kirurgija. V letih 1988–92 je bilo zdravljenih le 19 bolnikov in v letih 1993–97 le 17; povečanje relativnega petletnega preživetja iz 58% na 75% ni statistično značilno. Vseeno pa kaže, da se diagnostika in primarno zdravljenje izboljšujeta.

OSTEOGENI SARKOM

Pojavlja se pri mlajših, najpogosteje od 15–20 leta. V zadnjih 20 letih se je uspešnost zdravljenja zelo izboljšala. Pred obdobjem kemoterapije je bilo petletno preživetje lokalizirane bolezni zdravljene z amputacijo okoli 10%. Danes bolnike z lokalizirano boleznijo zdravimo z intenzivno kemoterapijo že pred operacijo. Tako se lahko v velikem odstotku izognemo amputaciji in kljub temu ozdravimo več kot polovico bolnikov (1, 2). Relativno petletno preživetje vseh bolnikov (tistih z omejeno in tistih z že ob diagnozi razsejano boleznijo) je bilo v letih 1988–92 17%, v letih 1993–97, ko se je intenzivna kemoterapija v kombinaciji z operacijo že dobro uveljavila, pa 53%. Z zdravljenjem, ki je trenutno na voljo, bomo verjetno ta odstotek težko izboljšali, morda le, če bi bili tumorji ob pričetku zdravljenja manjši.

EWINGOV SARKOM

Ker je ta vrsta kostnih sarkomov redka, spremembe relativnega petletnega preživetja bolnikov (7 v letih 1988–92, 6 v letih 1993–97) zaradi širokih intervalov zaupanja ne moremo vrednotiti. Zdravljenje Ewingovega sarkoma je kompleksno in dolgotrajno. Potrebni sta kemoterapija in operacija ter ponavadi še obsevanje.

V Sloveniji je v letih 1993–97 zbolelo zaradi vseh vrst primarnih kostnih tumorjev skupaj le 70 bolnikov. Ker so ti tumorji redki, jih večino zdravimo v Ljubljani na Onkološkem inštitutu, Pediatrični kliniki in Ortopedski kliniki. Prvo zdravljenje načrtujemo na konziliju. Rezultati zdravljenja so v zadnjem petletnem obdobju primerljivi z evropskimi (EUROCARE-3).

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From the data above it is evident that the bone sarcomas, such as chondrosarcomas, osteogenic sarcomas, and Ewing's sarcomas, are very rare and that they generally develop in young patients with the exception of chondrosarcomas.

CHONDROSARCOMA

Chondrosarcoma affects all age groups. The only treatment modality that yields cure is surgery. In the years 1988–92, only 19 patients were diagnosed with and treated for this sarcoma, and in the years 1993–97, only 17. An increase of the relative five-year survival from 58% to 75% is not statistically significant; nevertheless, it indicates that certain advances have been made in the diagnostics and primary treatment.

OSTEOGENIC SARCOMA

Osteogenic sarcoma is a malignant neoplasm affecting mainly adolescents aged between 15 and 20. In the last twenty years, the treatment outcome improved considerably. Before the era of chemotherapy, the five-year survival of patients with localized disease treated by amputation was 10%. Today, an intensive preoperative chemotherapy is applied to the patients with localized disease thereby allowing to avoid amputation to a large extent and still curing more than half of patients (1, 2). In the years 1988–92, the relative five-year survival of all patients, those with localized disease and others with advanced disease at diagnosis, was 17%, whereas in the years 1993–97, when the combined treatment of intensive chemotherapy and surgery was already widely used, it went up to 53%. This percentage can hardly be further improved by currently available treatment modalities or it can on condition that, at the beginning of the therapy, the tumors are of smaller size.

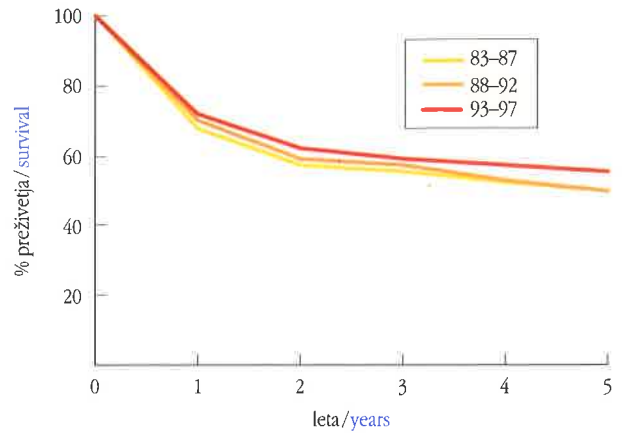
EWING'S SARCOMA

As this bone sarcoma is a rare malignancy, the difference of the relative five-year survival between the seven-year period 1988–92 and the six-year period 1993–97 is impossible to assess because rather wide confidence intervals. The treatment of Ewing's sarcoma is a very complex and long-lasting process. It usually involves chemotherapy, surgery and very often also radiotherapy.

In Slovenia, altogether 70 patients were affected with all types of primary bone tumors in the period 1993–97. As these tumors are rare, they are mainly treated in Ljubljana, at the Institute of Oncology, Department of Paediatrics of UMC or Department of Orthopaedic Surgery of UMC. Primary treatment plan is made by the multidisciplinary advisory team. The treatment results of the last observation period are comparable with the European ones (EUROCARE-3).

NE-HODGKINOVIM LIMFOMI

NON-HODGKIN LYMPHOMA



SLIKA 1: Relativno petletno preživetje bolnikov z ne-Hodgkinovimi limfomi, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of non-Hodgkin lymphoma patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za ne-Hodgkinovim limfomom (NHL) 1048 moških in 1052 žensk, od tega v letih 1993–97 442 moških in 466 žensk. Delež ektranodalnih lokacij je bil v celotnem obdobju 38%, v zadnjih letih pa 40%. V analizo ni bilo vključenih 45 (2%) bolnikov, ker je bil pri njih limfom ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca ne-Hodgkinovih limfomov močno večala. V letih 1983–87 je bila groba incidenčna stopnja 6,9/100.000 moških in 6,6/100.000 žensk, v letih 1993–97 pa 11,4/100.000 moških in 11/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnikov starejših od 55 let. Razširjenost bolezni ob diagnozi se je spremenila (tabela 2). Po letu 1987 je bilo več bolnikov odkritih v začetnem stadiju (I in II) bolezni.

V letih 1993–97 je bilo specifično zdravljenih 84% bolnikov. Prvo zdravljenje je bilo v največjem odstotku citostatsko (45%), v 33% kominirano: s kemoterapijo in obsevalno, v 11% samo obsevalno in v 11% samo kirurško. 84% bolnikov se je zdravilo na Onkološkem inštitutu v Ljubljani.

V letih 1993–97 je bilo relativno petletno preživetje za 5% večje kot v letih 1983–87 (slika 1). Preživetje se je izboljšalo v stadiju I in II (slika 2). Preživetje je bilo največje pri moških

In the period 1983–97, a total of 1,048 male and 1,052 female patients were diagnosed with non-Hodgkin lymphoma (NHL); of these, 442 males and 466 females were diagnosed in the period 1993–97. In the entire observation period, 38% of cases were extra-nodal and in the recent years, 40%. In 45 patients (2%), non-Hodgkin lymphoma was diagnosed at death; therefore, they were not included in the analysis.

In the observed 15-year period, the incidence of non-Hodgkin lymphoma was significantly increasing. In 1983–87, the crude incidence rate was 6.9/100,000 in males and 6.6/100,000 in females, whereas in 1993–97, it was 11.4/100,000 in males and 11/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In the observation period 1993–97, a higher number of patients aged over 55 years was observed. The stage distribution at diagnosis changed, too (Table 2). In the period following the year 1987, a higher percentage of patients with the disease in early stage (I and II) was noted.

In the period 1993–97, 45% of patients were treated by chemotherapy, 33% by chemo- and radiotherapy, 11% by radiotherapy alone, and 11% by surgery alone. 84% of patients were treated at the Institute of Oncology Ljubljana.

TABELA 1: Ne-Hodgkinovi limfomi. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Non-Hodgkin lymphoma. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Moški Males	1983-87	249	19	54	41	60	45	30
	1988-92	343	15	69	45	96	57	61
	1993-97	434	15	76	58	106	103	76
Ženske Females	1983-87	250	6	41	35	49	60	59
	1988-92	322	2	45	34	67	94	80
	1993-97	457	6	65	42	83	144	117

TABELA 2: Ne-Hodgkinovi limfomi. Bolniki vključeni v analizo po stadiju bolezni in obdobju opazovanja.

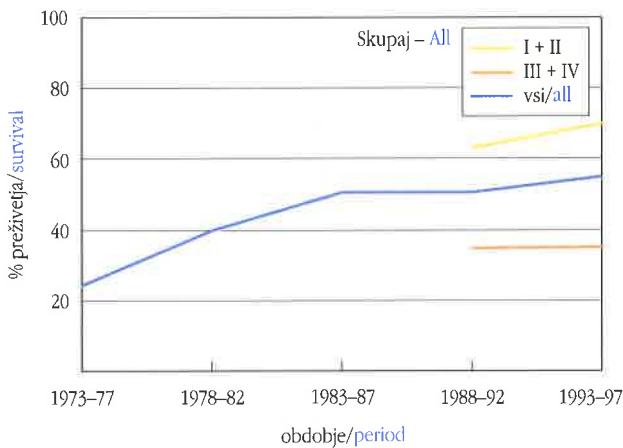
TABLE 2: Non-Hodgkin lymphoma. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage				Neznan/ Unknown	
		I+II	%	III+IV	%		%
1983-87	499	230	46,0	240	48,0	29	6,0
1988-92	665	346	52,0	254	38,0	65	10,0
1993-97	891	469	52,6	326	36,6	96	10,8

TABELA 3: Ne-Hodgkinovi limfomi. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).
TABLE 3: Non-Hodgkin lymphoma. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983–87	62	(56–68)	46	(40–52)	41	(34–48)	72	(66–78)	55	(48–62)	45	(38–52)
1988–92	69	(64–74)	52	(47–57)	42	(37–47)	66	(61–71)	50	(44–56)	42	(36–48)
1993–97	68	(64–72)	52	(47–57)	44	(39–49)	70	(66–74)	53	(48–58)	47	(42–52)

Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983–87	64	(58–70)	51	(44–58)	47	(40–54)	75	(69–81)	60	(54–66)	53	(46–60)
1988–92	72	(67–77)	58	(52–64)	51	(45–57)	68	(63–73)	55	(49–61)	50	(43–57)
1993–97	71	(66–76)	59	(54–64)	54	(48–60)	73	(69–77)	59	(54–64)	56	(50–62)



SLIKA 2: Relativno petletno preživetje bolnikov z ne-Hodgkinovimi limfomi, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.

FIGURE 2: Relative five-year survival of non-Hodgkin lymphoma patients diagnosed in the period 1973–1997 by stage and period of diagnosis.

v starosti 15–54 let, pri ženskah pa v starosti 45–64 let, najmanjše pa pri obeh spolih po 75. letu starosti (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje pri bolnikih z NHL pri moških 45,7% (44,3–47,2) in pri ženskah 51,3% (49,9–52,7), v Sloveniji pa pri moških 46,1% (39,2–54,2) in pri ženskah 45,4% (39,3–52,5). Največje preživetje pri moških in pri ženskah je bilo na Tirolskem v Avstriji: 62,1% oziroma 74,1%.

Marjeta Vovk, Onkološki inštitut Ljubljana

Ne-Hodgkinovi limfomi so raznolika skupina bolezenskih enot, ki se kaže v morfološki in imunofenotipski raznolikosti, različnem poteku, odzivu na zdravljenje in prognozi (1).

The relative five-year survival rate was 5% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The survival improved in stages I and II (Figure 2). In men, the survival rate was the highest in the age group of 15–54 years and in women in the age group of 45–64 years. In both sexes, the patients over 75 years had the poorest survival (Figure 3).

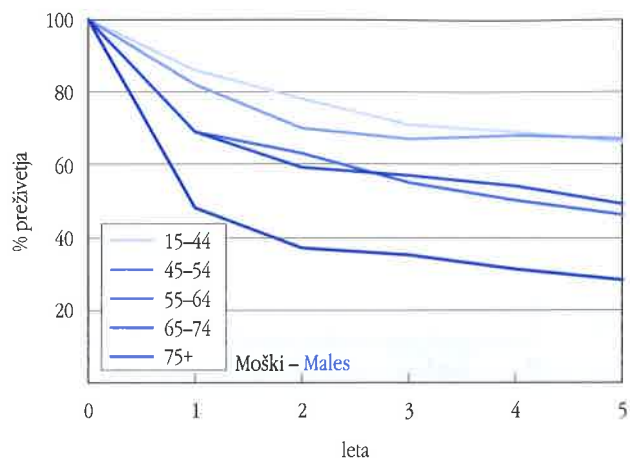
According to the EURO CARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with non-Hodgkin lymphoma was 45.7% (44.3–47.2) in male patients and in female patients 51.3% (49.9–52.7), while in Slovenia, it was 46.1% (39.2–54.2) in male patients and 45.4% (39.3–52.5) in female patients. The highest rates of 62.1% in male and of 74.1% in female patients were observed in Tyrol in Austria, respectively.

Marjeta Vovk, Institute of Oncology Ljubljana

Non-Hodgkin lymphomas are a heterogeneous group of disease, distinguishing from each other by morphology, immunophenotyping, course of the disease, response to treatment and prognosis (1).

The reason why a long story of searching for new forms of lymphomas and their categorization by histologic type has not been concluded, lies in a rapid progress of immunology, molecular biology and cytogenetics. In the 1980s, a modified Kiel's classification was in use, and in the 1990s, a revised European-American classification of lymphomas (REAL).

After 1983, the selection of treatment modality of non-Hodgkin lymphomas was made according to the histologic type of NHL. Indolent lymphomas are treated by non-aggressive chemotherapy with one or more cytostatics, in combination with radiotherapy or without it, but only when the symptoms are present. Aggressive lymphomas are treated by chemotherapy immediately after the diagnosis. The selection of treatment schedule depends on the histology subtype of NHL (CHOP, ACVBP, BFM). Chemotherapy can be applied in combination with or



SLIKA 3: Relativno petletno preživetje bolnikov z ne-Hodgkinovimi limfomi, zbolelih v letih 1993–1997 po starosti.

Hiter razvoj imunologije, molekularne biologije in citogenetike je razlog, da dolga zgodba o iskanju novih oblik limfomov in njihovem razvrščanju po histološkem tipu še ni končana. V 80. letih smo uporabljali modificirano Kielsko klasifikacijo, v drugi polovici 90. pa Revidirano evropsko ameriško klasifikacijo limfoidnih novotvorb (REAL).

Po letu 1983 smo zdravljenje prilagodili histološkemu tipu NHL. Indolentne limfome zdravimo le ob simptomih z neagresivno kemoterapijo, torej z enim ali več citostatiki in z obsevanjem ali brez njega. Agresivne limfome pa zdravimo takoj ob diagnozi s kemoterapijo, izbor katere je odvisen od histološke podvrste NHL (CHOP, ACVBP, BFM) ter z obsevanjem ali brez njega. Način zdravljenja se torej v opazovanem obdobju ni bistveno spremenil (2, 3).

Izboljšanje 5-letnega preživetja v letih 1993–97 je posledica natančnejše histološke opredelitve, histološkemu podtipu prilagojenega zdravljenja in boljšega podpornega zdravljenja (npr. uporaba granulocitnega ravnega faktorja od prve polovice 90. let, boljšega obvladovanja okužbe itd).

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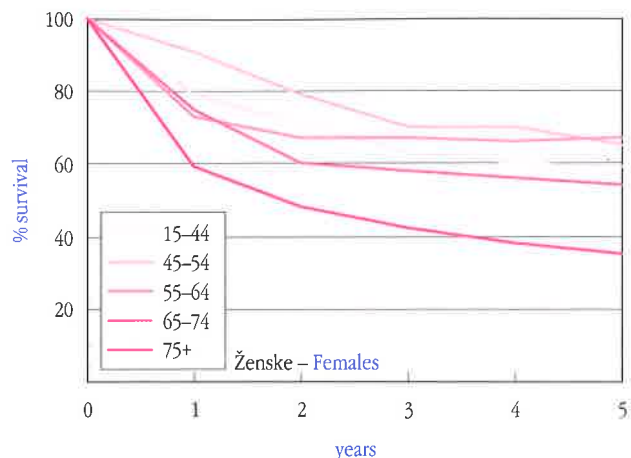


FIGURE 3: Relative five-year survival of non-Hodgkin lymphoma patients diagnosed in the period 1993–1997 by age.

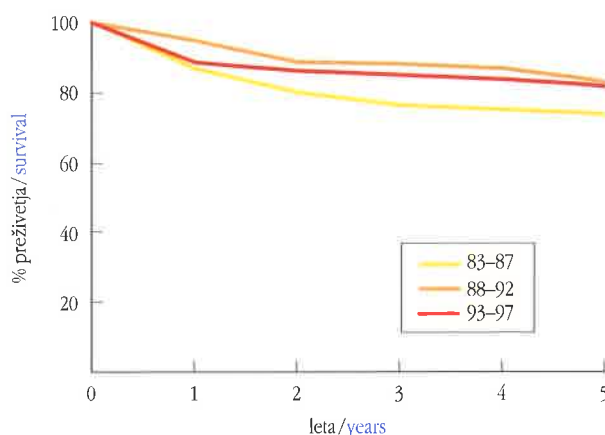
without radiotherapy. The treatment modality did not change much in the observed period (2, 3).

An improvement in five-year survival in the observation period 1993–97 resulted from a more accurate histology classification, histology subtype-adjusted treatment and improved supportive treatment, e. g. the use of the granulocyte growth factor since the first mid of the 1990, better management of infection, etc.

HODGKINOV LIMFOM

HODGKIN LYMPHOMA

MKB 8/ICD 8: 201



SLIKA 1: Relativno petletno preživetje bolnikov s Hodgkinovim limfomom, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of Hodgkin lymphoma patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za Hodgkinovim limfomom 326 moških in 245 žensk, od tega v letih 1993–97 106 moških in 93 žensk. V analizo ni bilo vključenih 14 (2,5%) bolnikov, ker je bil pri njih limfom ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju je bila incidenca Hodgkinovega limfoma ustaljena. V letih 1983–87 je bila groba incidenčna stopnja 2,4/100.000 moških in 1,5/100.000 žensk, v letih 1993–97 pa 2,2/100.000 moških in 1,8/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnikov v starostni skupini 15–44 let. Razširjenost bolezni ob diagnozi se ni pomembno spremenila, le v letih 1988–92 je bilo nekoliko več bolezni odkrite v začetnem stadiju (tabela 2).

V letih 1993–97 je bilo zdravljenih 96% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (44%) kombinirano: obsevalno in citostatsko, v 42% samo citostatsko, v 13% samo obsevalno. V 85% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 11% na Pediatrični kliniki in v 2% v Mariboru in v 1% v Celju.

V letih 1993–97 je bilo relativno petletno preživetje za 8% večje kot v letih 1983–87 (slika 1). Največje spremembe v preživetju so bile v stadiju III in IV pri obeh spolih (slika 2). Preživetje je bilo največje pri otrocih in odraslih do 54. leta

In the period 1983–97, a total of 326 male and 245 female patients were diagnosed with Hodgkin lymphoma; of these, 106 males and 93 females were diagnosed in the period 1993–97. In 14 patients (2.5%), Hodgkin lymphoma was diagnosed at death; therefore, they were not included in the analysis.

In the observed 15-year period, the incidence of Hodgkin lymphoma was steady. In 1983–87, the crude incidence rate was 2.4/100,000 in males and 1.5/100,000 in females, whereas in 1993–97, it was 2.2/100,000 in males and 1.8/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In the observation period 1993–97, a higher number of patients was observed in the age group of 15–44 years. The stage distribution at diagnosis has not significantly changed. Only in the period 1988–92, a higher percentage of patients with the disease in early stage was noted (Table 2).

In the period 1993–97, 96% of patients underwent specific treatment. In most cases (44%), primary treatment was combined chemotherapy and radiotherapy, 42% of patients were treated by chemotherapy alone, and 13% by radiotherapy alone. Primary treatment was started at the Institute of Oncology Ljubljana in 85% of patients, in 11% at the Department of

TABELA 1: Hodgkinov limfom. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Hodgkin lymphoma. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi/ Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	105	13	53	13	14	7	5
Males	1988-92	107	15	58	14	13	5	2
	1993-97	104	8	65	8	12	7	4
Ženske	1983-87	72	8	33	5	5	12	9
Females	1988-92	76	5	51	3	8	7	2
	1993-97	93	7	56	5	6	11	8

TABELA 2: Hodgkinov limfom. Bolniki vključeni v analizo po stadiju bolezni in obdobju opazovanja.

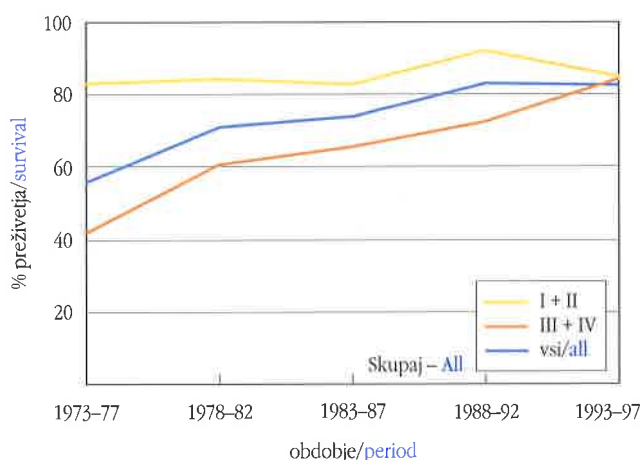
TABLE 2: Hodgkin lymphoma. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij/Stage				Neznan/ Unknown	
		I+II	%	III+IV	%		%
1983-87	177	90	51,0	85	48,0	2	1,0
1988-92	183	100	55,0	83	45,0	0	
1993-97	197	94	48,0	95	48,0	8	4,0

TABELA 3: Hodgkinov limfom. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Hodgkin lymphoma. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983–87	88	(82–94)	73	(64–82)	67	(58–76)	82	(73–91)	72	(61–83)	69	(58–80)
1988–92	93	(88–98)	82	(75–89)	75	(67–83)	96	(92–100)	91	(84–98)	86	(78–94)
1993–97	89	(83–95)	83	(76–90)	79	(71–87)	86	(79–93)	82	(74–90)	77	(68–86)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years					Ženske/Females Leta/Years						
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983–87	89	(82–96)	76	(67–85)	72	(62–82)	83	(74–92)	76	(65–87)	76	(64–88)
1988–92	94	(89–99)	84	(76–92)	79	(70–88)	67	(63–71)	92	(85–99)	88	(80–96)
1993–97	91	(85–97)	86	(78–94)	84	(75–93)	87	(80–94)	84	(76–92)	81	(72–90)



SLIKA 2: Relativno petletno preživetje bolnikov s Hodgkinovim limfomom, zbolelih v letih 1973–1997 po stadiju in obdobju diagnoze.

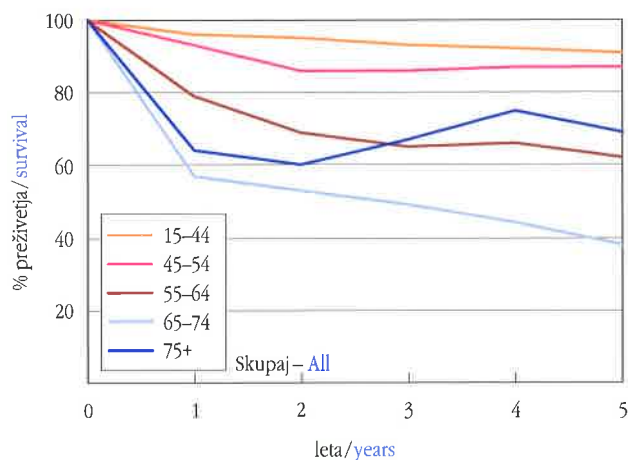
FIGURE 2: Relative five-year survival of Hodgkin lymphoma patients diagnosed in the period 1973–1997 by stage and period of diagnosis.

starosti (87–91 %) (slika 3). Ocena preživetja bolnikov, starejših od 55 let, je nezanesljiva zaradi majhnega števila primerov v posameznih starostnih skupinah (tabela 1).

Izsledki študije EUROCARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje bolnikov s Hodgkinovim limfomom pri moških 73,5 % (71–76,2) in pri ženskah 80,2 % (78,1–82,2), v Sloveniji pa pri moških 75,6 % (65,7–86,8) in pri ženskah 76,2 % (70,7–82,2). Največje preživetje pri moških je bilo 89,5 % na Tirolskem v Avstriji in pri ženskah 90,9 % na območjih registrov Basla in Ženeve v Švici.

Marjeta Vovk, Onkološki inštitut Ljubljana

Pomembna mejnika v diagnostiki Hodgkinovega limfoma sta bila uvedba računalniške tomografije prsnega koša in trebuha (1981) ter ultrazvočne preiskave trebuha (1984). Preiskavi omogočata natančnejšo določitev stadijev.



SLIKA 3: Relativno petletno preživetje bolnikov s Hodgkinovim limfomom, zbolelih v letih 1993–1997 po starosti.

FIGURE 3: Relative five-year survival of Hodgkin lymphoma patients diagnosed in the period 1993–1997 by age.

Paediatrics, UMC in Ljubljana, in 2% in the General Hospital in Maribor, and in 1% in the General Hospital in Celje.

The relative five-year survival rate was 8% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The major changes in survival occurred in the disease stages III and IV in both sexes (Figure 2). The survival was the highest in children and adults under 54 (87–91%) (Figure 3). The estimated survival rate of patients aged over 55 is not reliable because of a small number of cases in each individual age group (Table 1).

According to the EUROCARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with Hodgkin lymphoma was 73.5% (71–76.2) in male patients and in female patients 80.2% (78.1–82.2), while in Slovenia, it was 75.6% (65.7–86.8) in male patients and 76.2% (70.7–82.2) in female patients. The highest rates of 89.5% in male and of 90.9% in female patients were observed in Tyrol in Austria and Switzerland (only registries Basle and Geneva), respectively.

S postopnim prepoznavanjem prognostičnih dejavnikov (stadij, velikost tumorske mase, sedimentacijo eritrocitov, B simptomi itd.) so se v 80. in 90. letih dopolnjevala merila za izbor načina zdravljenja, ki upošteva prognostične dejavnike. Že znano učinkovito kombinacijo citostatikov po shemi MOPP z veliko poznih sopojavov smo zamenjali z enako ali bolj učinkovitimi kemoterapevtskimi shemami z manj poznih sopojavov: ABVD (1980), MOPP/ABVD (1985), MOPP/ABV (1987) in kasneje BEACOPP (1997). Vse doslej naštetu je omogočilo uvedbo kombiniranega zdravljenja v poznih 80. in začetku 90. let, kar pomeni začetek zdravljenja s kemoterapijo, nadaljevanje z obsevanjem prizadetih regij pri začetnem stadiju (I in II) in obsevanje eventualnega ostanka pri napredovanem stadiju (III in IV). Obsevalna doza je odvisna od učinka kemoterapije. Zdravljenje Hodgkinovega limfoma samo z obsevanjem z velikim obsevalnim poljem in dozo je preteklost.

Naštete spremembe v diagnostiki, osnovnem in podpornem zdravljenju so vzrok dobrim rezultatom tudi pri napredovanih stadijih (1).

VIR

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Marjeta Vouk, Institute of Oncology Ljubljana

Computer tomography of the chest and abdomen introduced in 1981 and US examination of the abdomen in 1984 are two important landmarks in the diagnostics of Hodgkin lymphoma. Both methods allow an accurate determination of the disease stage.

Establishing gradually the prognostic factors, viz. stage, size of tumor mass, erythrocyte count, B-symptoms, etc., the guidelines for treatment choice, taking into account also the prognostic factors, were being updated in the 1980s and 1990s. An effective and most functional combination of cytostatics according to MOPP schedule that was known to have a high number of late toxic effects, was replaced by a similar, yet more effective treatment schedules with less late toxic effects. These are ABV (1980), MOPP/ABVD (1985), MOPP/ABV (1987), and later on, in 1997, also BEACOPP. The above treatment schedules facilitated the application of combined treatment in the late 1980s and early 1990s. The treatment of the disease stages I and II is started with chemotherapy and continued by irradiation of the affected regions. In more advanced stages (III and IV), eventual residual disease is treated by irradiation. The irradiation dose depends on the efficiency of chemotherapy. The treatment of Hodgkin lymphoma by radiotherapy alone, applying large irradiation fields and high doses, is out-of-date.

The advances in diagnostics, primary and supportive treatment contributed considerably to the better treatment results also in more advanced stages of the disease (1).

AKUTNA LIMFOBLASTNA LEVKEMIJA

ACUTE LYMPHOBLASTIC LEUKEMIA

MKB 8/ICD 8: 2040

V obdobju 1983–97 je zbolelo za akutno limfoblastno levkemijo (ALL) 168 moških in 159 žensk, od tega v letih 1993–97 57 moških in 50 žensk. V analizo nista bila vključena 2 (1%) bolnika, ker je bila pri njiju levkemija ugotovljena šele ob smrti.

V opazovanem 15-letnem obdobju se incidenca akutne limfoblastne levkemije ni pomembno spremenila. V letih 1983–87 je bila groba incidenčna stopnja 1,2/100.000 moških in 0,9/100.000 žensk, v letih 1993–97 pa 1,2/100.000 moških in 1/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V zadnjih letih je bilo odkritih več bolnikov v starosti 65–74 let. V starosti 0–4 let se število novih bolnikov ni povečalo, povečala pa se je starostno specifična stopnja incidence.

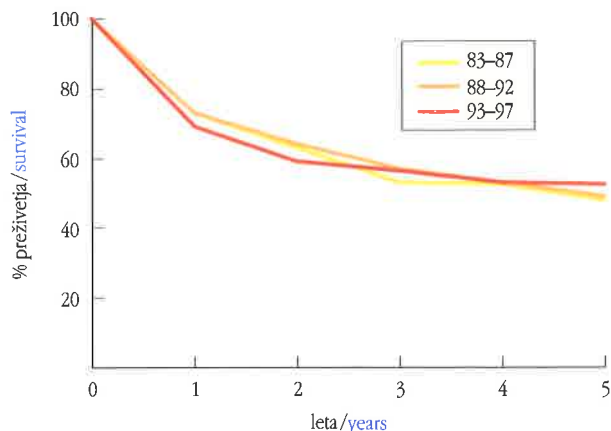
V letih 1993–97 je bilo specifično zdravljenih 72% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (62%) samo citostatsko, v 37% citostatsko in obsevalno. V 78% so pričeli s prvim zdravljenjem na Pediatrični kliniki KC v Ljubljani, v 14% na Kliničnem oddelku za hematologijo KC, v 7% na Onkološkem inštitutu v Ljubljani in v 1% v SB v Mariboru.

V letih 1993–97 je bilo relativno tri in petletno preživetje za 4% večje kot v letih 1983–87. Enoletno preživetje je bilo za 4% manjše (slika 1). Spremembe v preživetju so bile večje pri otrocih (1993–97) in pri mladih odraslih (obdobje 1988–92) kot pri starejših (slika 2).

TABELA 1: Akutna limfoblastna levkemija. Bolniki vključeni v analizo po starosti in obdobju opazovanja.

TABLE 1: Acute lymphoblastic leukemia. Patients included in the analysis by age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15-44	45-54	55-64	65-74	75+	
Skupaj	97	56	27	4	5	1	4	
All	123	62	38	7	7	5	4	
	1993-97	105	52	23	8	7	12	3



SLIKA 1: Relativno petletno preživetje bolnikov z akutno limfoblastno levkemijo, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of acute lymphoblastic leukemia patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 168 male and 159 female patients were diagnosed with acute lymphoblastic leukemia (ALL); of these, 57 males and 50 females were diagnosed with this cancer in the period 1993–97. In 2 patients (1%), acute lymphoblastic leukemia was diagnosed at death; therefore, they were not included in the analysis.

In the observed 15-year period, the incidence of acute lymphoblastic leukemia did not significantly change. In 1983–87, the crude incidence rate was 1.2/100,000 in males and 0.9/100,000 in females, whereas in 1993–97, it was 1.2/100,000 in males and 1/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In the observation period 1993–97, a higher number of patients was observed in the age group of 65–74 years. In the age group of 0–4 years, the number of newly detected patients did not increase, whereas the age-specific incidence rate did.

In the period 1993–97, 72% of patients underwent specific treatment. In most cases (62%), primary treatment was chemotherapy alone; 37% of patients were treated by radiotherapy and chemotherapy. Primary treatment was started at the Department of Paediatrics, UMC, Ljubljana in 78% of patients, in 14% at the Department of Haematology, UMC, Ljubljana, in 7% at the Institute of Oncology Ljubljana, and in 1% in the General Hospital in Maribor.

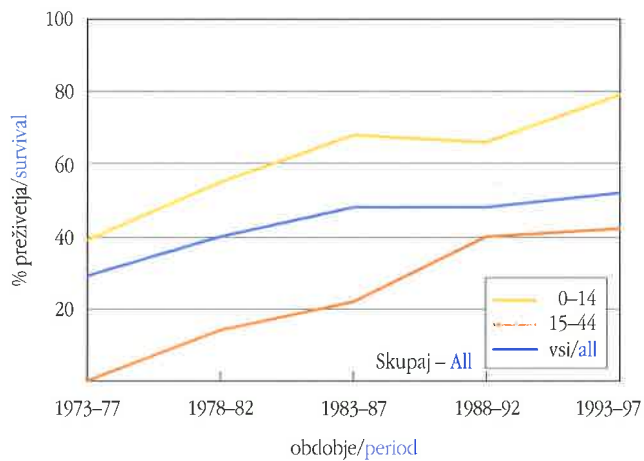
The relative five-year survival rate was 4% higher in the years 1993–97 than in the years 1983–87. The one-year survival decreased by 4% (Figure 1). Bigger changes in survival were observed in children (1993–97) and in young adults (1988–92) than in elderly (Figure 2).

According to the EURO CARE-3 study results for the period 1990–94 in Europe the age-standardized relative survival rate of adult patients with ALL was 27.2% (22.9–32.3) in male patients and in female patients 24.9% (19.9–31.1), while in Slovenia, it was 16.3% (7.3–36.4) in male patients and 36.1% (23.2–56.1) in female patients. The highest rates of 45.4% in adult male and of 55.9% in female patients were observed

TABELA 3: Akutna limfoblastna levkemija. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Acute lymphoblastic leukemia. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	76	(65-87)	51	(38-64)	47	(34-60)	67	(52-82)	52	(37-67)	45	(30-60)
1988-92	73	(61-85)	64	(51-77)	57	(44-70)	72	(61-83)	49	(37-61)	40	(28-52)
1993-97	75	(64-86)	58	(46-72)	50	(37-63)	60	(46-74)	50	(36-64)	48	(34-62)

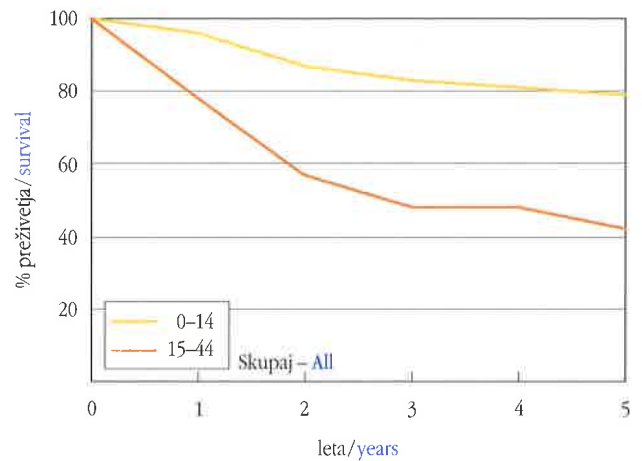
Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	77	(65-89)	52	(38-66)	49	(35-63)	67	(52-82)	54	(38-70)	47	(31-63)
1988-92	74	(62-86)	65	(52-78)	59	(45-73)	72	(61-83)	50	(38-62)	41	(29-53)
1993-97	76	(65-87)	59	(46-72)	52	(38-66)	61	(47-75)	51	(36-66)	50	(35-65)

**SLIKA 2: Relativno petletno preživetje bolnikov z akutno limfoblastno levkemijo, zbolelih v letih 1973-1997 po starosti in obdobju diagnoze.****FIGURE 2: Relative five-year survival of acute lymphoblastic leukemia patients diagnosed in the period 1973-1997 by age and period of diagnosis.**

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje odraslih bolnikov z ALL pri moških 27,2% (22,9-32,3) in pri ženskah 24,9% (19,9-31,1), v Sloveniji pa pri moških 16,3% (7,3-36,4) in pri ženskah 36,1% (23,2-56,1). Največje preživetje pri moških je bilo 45,4% v Nemčiji (samo Posarje) in pri ženskah 55,9% v Španiji v provincah: Baskija, Mallorca, Navarra in Tarragona.

Jožica Anžič, *Pediatrična klinika KC*

Možna razlaga za višje tri in petletno preživetje je razvoj novih diagnostičnih metod in doslednejša uporaba kriterijev za boljše razlikovanje podskupin bolezni glede na njihovo biološko agresivnost in stopnji rizika za ponovitev bolezni prirejena intenzivnost zdravljenja.

**SLIKA 3: Relativno petletno preživetje bolnikov z akutno limfoblastno levkemijo, zbolelih v letih 1993-1997 po starosti.****FIGURE 3: Relative five-year survival of acute lymphoblastic leukemia patients diagnosed in the period 1993-1997 by age.**

respectively in Germany (Saarland only) and Spain (only regions: Basque Country, Mallorca, Navarra and Tarragona).

Jožica Anžič, *Department of Paediatrics, UMC, Ljubljana*

A possible explanation for the improvement in three- and five-year survival rate is the progress made in diagnostics and consistency in following the guidelines for a more exact differentiation of the disease subgroups by the grade of biological aggressiveness, and the intensity of the therapy adjusted to the risk of relapse.

A decline in one-year survival may be attributed to a more aggressive therapy that, the first year after the diagnosis or soon after the beginning of the therapy, increases the death risk in patients with unfavorable prognostic factors. These patients

Nižje enoletno preživetje pa gre lahko na račun intenzivnejšega zdravljenja, ki pri bolnikih z bolj neugodnimi prognozičnimi kazalci poveča umrljivost v prvem letu po diagnozi oz. začetku zdravljenja. Ti bolniki so verjetno prej vplivali na večjo umrljivost v obdobju do pet let (1, 2).

Sicer pa se načini zdravljenja: kombinacija citostatikov, način zaščite centralnega živčnega sistema v proučevanem obdobju niso pomembno spreminjali in zato verjetno niso vzrok spremembam v preživetju.

Jože Pretnar, Klinični oddelek za hematologijo KC

V zadnjih letih je vse več bolnikov starejših od 65 let, vendar jih je še vedno malo. V obdobju od 1989 do 2000 smo opravili 13 alogeničnih presaditev kostnega mozga, pri njih pričakujemo okrog 70% 10-letno preživetje (3).

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2. Mali P, Jazbec J. Preživetje otrok in mladostnikov z akutno levkemijo v Sloveniji v obdobju 1990–1999. Slov Pediatr 2002; 9: 86–9.
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might have had an effect on the rise of five-year mortality rate (1, 2).

Treatment modalities have not considerably changed, combining more or less the same cytostatics and protection methods for the central nervous system; they therefore could not have any impact on the changes in the survival.

Jože Pretnar, Department of Haematology, UMC, Ljubljana

In recent years, more patients with ALL fall into the age group over 65 years, though they are still not so many. In the period 1989–2000, 13 allogeneic bone marrow transplantations were performed. The 10-year survival of these patients is expected to be about 70% (3).

AKUTNE NELIMFOBLASTNE LEVKEMIJE

ACUTE NON-LYMPHOBLASTIC LEUKEMIAS

MKB 8 / ICD 8: 2050, 2060, 2070

V obdobju 1983–97 je zbolelo za akutno nelimfoblastno levkemijo 310 moških in 300 žensk, od tega v letih 1993–97 127 moških in 102 ženske. V analizo ni bilo vključenih 29 (5%) bolnikov, ker je bila pri njih levkemija ugotovljena šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca akutne nelimfoblastne levkemije pri moških večala. V letih 1983–87 je bila groba incidenčna stopnja 1,4/100.000 moških in 2/100.000 žensk, v letih 1993–97 pa 2,6/100.000 moških in 2/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več moških, starih 55 let in več, ter več žensk, starih 65 let in več.

V letih 1993–97 so v 84% pričeli s prvim zdravljenjem na Kliničnem oddelku za hematologijo KC v Ljubljani, v 9% na Pediatrični kliniki KC, v 4% v SB v Mariboru. Po en bolnik je bil zdravljen v SB v Celju, Murski Soboti in Šempetru pri Novi Gorici.

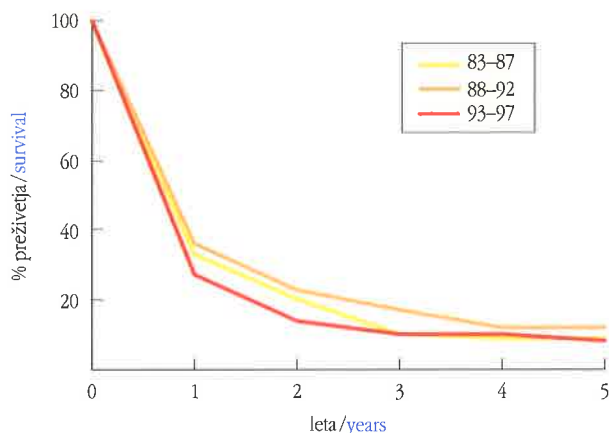
V opazovanem obdobju je bilo relativno petletno preživetje največje v letih 1988–92 (slika 1). Preživetje se je v letih 1993–97 povečalo samo pri otrocih (na 40%). V vseh drugih starostnih skupinah je bilo manjše od 20%. Najmanjše je bilo po 65. letu starosti in pri mladih odraslih, starih od 15–44 let (slika 3).

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje

TABELA 1: Akutne nelimfoblastne levkemije. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Acute non-lymphoblastic leukemias. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	63	10	11	9	11	14	8
Males	1988-92	114	6	24	16	28	21	19
	1993-97	123	4	17	20	29	33	20
Ženske	1983-87	94	5	23	10	20	17	19
Females	1988-92	93	9	20	11	17	13	23
	1993-97	94	1	19	12	16	21	25



SLIKA 1: Relativno petletno preživetje bolnikov z akutno nelimfoblastno levkemijo, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of acute non-lymphoblastic leukemia patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 310 male and 300 female patients were diagnosed with acute non-lymphoblastic leukemia; of these, 127 males and 102 females were diagnosed in the period 1993–97. In 29 patients (5%), acute non-lymphoblastic leukemia was diagnosed at death; therefore, they were not included in the analysis.

In the observed 15-year period, the incidence of acute non-lymphoblastic leukemia was increasing in men. In 1983–87, the crude incidence rate was 1.4/100,000 in males and 2/100,000 in females, whereas in 1993–97, it was 2.6/100,000 in males and 2/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In the observation period 1993–97, there were more male patients aged over 55 and more female patients aged over 65 years.

In 1993–97, primary treatment was started at the Department of Haematology, UMC, Ljubljana in 84% of patients, in 9% of patients at the Department of Paediatrics, UMC, Ljubljana, in 4% in General Hospital in Maribor; in each of General Hospitals in Celje, Murska Sobota and Šempeter pri Novi Gorici, primary treatment was started in one patient.

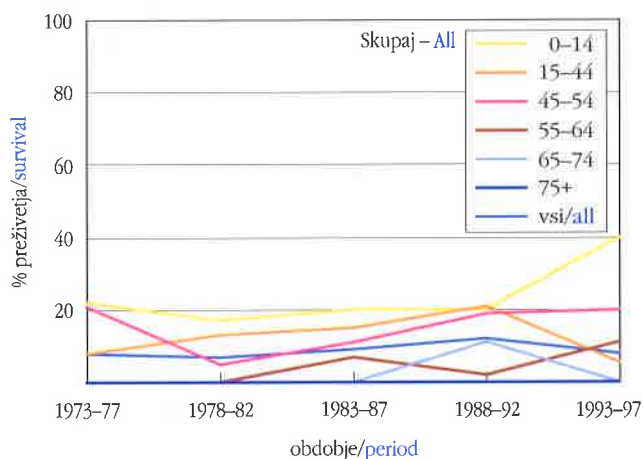
In the whole observation period, the relative five-year survival rate was the highest in the years 1988–92 (Figure 1). In the years 1993–97, the survival increased only in children (by 40%). In all other age groups, it dropped and was less than 20%. The poorest survival was observed in the patients older than 65 year and in young adults aged 15–44 years (Figure 3).

According to the EURO CARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the adult patients with acute non-lymphoblastic leukemia was 9.3% (7.8–11.1) in male patients and in female patients 10.6% (8.9–12.6), while in Slovenia, it was 9.2% (4.6–18.4) in male patients and 7.6% (3.3–17.4) in female patients. The highest rates of 15.1% in male and of 21.2% in female patients were observed in Switzerland (only registries in Basle and Geneva) and Finland, respectively.

TABELA 3: Akutne nelimfoblastne levkemije. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Acute non-lymphoblastic leukemias. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	37	(25-49)	6	(1-11)	6	(1-11)	29	(20-38)	11	(5-17)	9	(3-15)
1988-92	32	(23-41)	11	(5-17)	8	(3-13)	39	(29-49)	19	(11-27)	13	(6-20)
1993-97	24	(16-32)	9	(4-14)	7	(2-12)	28	(19-37)	10	(4-16)	5	(1-9)

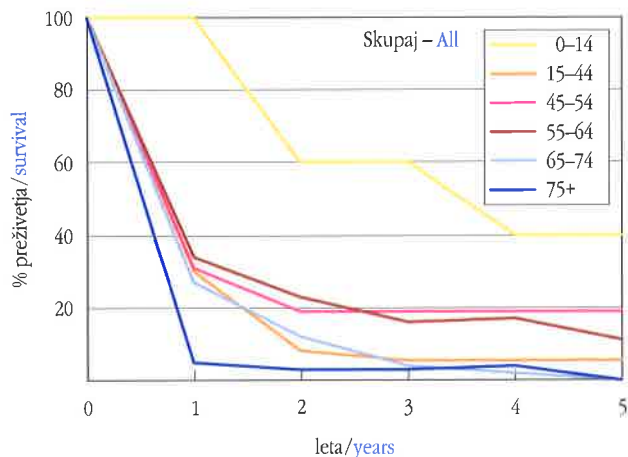
Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	38	(25-51)	7	(1-13)	7	(1-13)	29	(19-39)	11	(4-18)	10	(3-17)
1988-92	33	(24-42)	13	(6-20)	10	(4-16)	40	(30-50)	21	(12-30)	15	(7-23)
1993-97	25	(17-33)	10	(4-16)	9	(3-15)	29	(19-39)	11	(4-18)	6	(1-11)

**SLIKA 2: Relativno petletno preživetje bolnikov z akutno nelimfoblastno levkemijo, zbolelih v letih 1973-1997 po starosti in obdobju diagnoze.****FIGURE 2: Relative five-year survival of acute non-lymphoblastic leukemia patients diagnosed in the period 1973-1997 by age and period of diagnosis.**

odraslih bolnikov z akutno mieloično levkemijo pri moških 9,3% (7,8-11,1) in pri ženskah 10,6% (8,9-12,6), v Sloveniji pa pri moških 9,2% (4,6-18,4) in pri ženskah 7,6% (3,3-17,4). Največje preživetje pri moških je bilo 15,1% v Švici na območju registrov Basel in Ženeva in pri ženskah 21,2% na Finskem.

Jože Pretnar, Klinični oddelek za hematologijo KC

Podatek o tem, da se v zadnjih petih letih preživetje ni izboljšalo, oziroma se je celo nekoliko poslabšalo, je presenetljiv (1, 2, 3, 4). V obdobju od 1989 do 2000 smo opravili 25 alogeničnih transplantacij perifernih krvotvornih matičnih celic. 10 letno preživetje naj bi bilo okrog 55%, če pa upoštevamo bolnike, ki so imeli presaditev v prvi remisiji, pa okrog 80%.

**SLIKA 3: Relativno petletno preživetje bolnikov z akutnimi nelimfoblastnimi levkemijami, zbolelih v letih 1993-1997 po starosti.****FIGURE 3: Relative five-year survival of acute non-lymphoblastic leukemia patients diagnosed in the period 1993-1997 by age.**

Jože Pretnar, Department of Haematology, UMC, Ljubljana

The data showing that, in the last five years, the survival has not improved, but rather declined, is truly most surprising (1, 2, 3, 4). In the period 1989-2000, we performed 25 allogeneic peripheral hematopoietic stem-cell transplantations. The expected 10-year survival should be 55%; however, taking into account also the patients who underwent transplantation at the first remission, the expected 10-year survival might be about 80%. It is surprising that the survival was the poorest in the age group of 15-44 years, *i.e.* the group in which, according to the data from the literature, the best treatment results were obtained with allogeneic peripheral hematopoietic stem-cell transplantations as well as with standard chemotherapy.

Preseneča ugotovitev, da je preživetje najslabše prav v starostni skupini 15–44 let, to je v skupini, ki ima po podatkih iz literature najboljše rezultate zdravljenja z alogenično transplantacijo perifernih krvotvornih matičnih celic, kakor tudi s konvencionalno kemoterapijo.

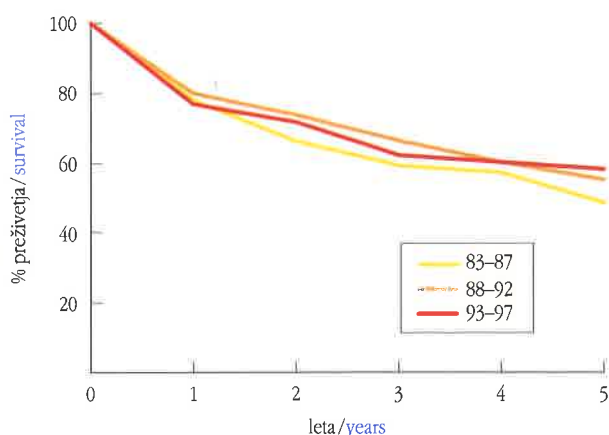
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KRONIČNA LIMFOCITNA LEVKEMIJA

CHRONIC LYMPHOCYTIC LEUKEMIA

MKB 8 / ICD 8: 2041



SLIKA 1: Relativno petletno preživetje bolnikov s kronično limfocitno levkemijo, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of chronic lymphocytic leukemia patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za kronično limfocitno levkemijo (KLL) 559 moških in 460 žensk, od tega v letih 1993–97 210 moških in 152 žensk. V analizo ni bilo vključenih 62 (6%) bolnikov, ker je bila pri njih levkemija ugotovljena šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca KLL večala. V letih 1983–87 je bila groba incidenčna stopnja 3,8/100.000 moških in 2,7/100.000 žensk, v letih 1993–97 pa 4,4/100.000 moških in 3/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V zadnjih letih je bilo odkritih več moških v starosti 65 let in več žensk v starosti 55–64 let.

V letih 1993–97 je bilo specifično zdravljenih samo 38% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (82%) samo citostatsko, v 10% samo obsevalno, v 4% obsevalno in citostatsko. V 33% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 18% v SB v Šempetru pri Novi Gorici, v 13% v SB v Celju, v 12% v SB v Mariboru, v 7% na Kliničnem oddelku za hematologijo KC v Ljubljani, v 7% v SB v Slovenj Gradcu, v 6% v SB v Murski Soboti, po 1% v SB na Jesenicah, v SB v Novem Mestu in v Trbovljah.

V letih 1993–97 je bilo relativno petletno preživetje za 10% večje kot v letih 1983–87 (slika 1). Preživetje se je največ povečalo v starostnih skupinah 45–54 let in več kot 75 let (slika 2).

TABELA 1: Kronična limfocitna levkemija. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Chronic lymphocytic leukemia. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	172	0	6	29	36	51	50
Males	1988-92	160	0	8	21	41	49	41
	1993-97	194	0	5	14	50	61	64
Ženske	1983-87	130	0	3	9	22	40	56
Females	1988-92	163	0	4	10	32	54	63
	1993-97	138	0	1	11	34	47	45

In the period 1983–97, a total of 559 male and 460 female patients were diagnosed with chronic lymphocytic leukemia; of these, 210 males and 152 females were diagnosed in the period 1993–97. In 62 (6%) patients, chronic lymphocytic leukemia was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of chronic lymphocytic leukemia was increasing. In the period 1983–87, the crude incidence rate was 3.8/100,000 in males and 2.7/100,000 in females, whereas in 1993–97, it was 4.4/100,000 in males and 3/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In the observation period 1993–97, more chronic lymphocytic leukemia cases were detected in the male patients older than 65 years and female patients in the age group 55–64.

In the period 1993–97, 38% of patients underwent specific treatment. In most cases (82%), primary treatment was chemotherapy alone, 10% of patients were treated by radiotherapy alone, and 4% by radiotherapy and chemotherapy. Primary treatment was started at the Institute of Oncology Ljubljana in 33% of patients, in 18% in the General Hospital in Šempeter pri Novi Gorici, in 13% in the General Hospital in Celje, in 12% in the General Hospital in Maribor, in 7% at the Department of Haematology, UMC, Ljubljana, in 7% in the General Hospital in Slovenj Gradec, in 6% in the General Hospital in Murska Sobota, in 1% in each of General Hospitals in Jesenice, in Novo mesto and in Trbovlje.

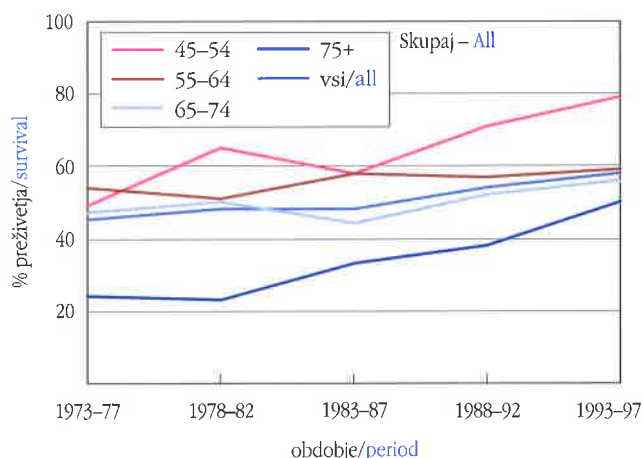
The relative five-year survival rate was 10% higher in the years 1993–97 than in the years 1983–87 (Figure 1). The highest increase in survival was observed in the age groups of patients of 45–54 years and in those older than 75 years (Figure 2). In the age group of 45–54 years the survival was 29% higher than in the group of patients over 75 years old (Figure 3). In all three observation periods, the survival was higher in female than in male patients.

According to the EURO CARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival

TABELA 3: Kronična limfocitna levkemija. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Chronic lymphocytic leukemia. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	73	(66-80)	48	(40-56)	30	(23-37)	75	(67-83)	52	(43-61)	43	(34-52)
1988-92	78	(71-85)	54	(46-62)	38	(30-46)	75	(68-82)	59	(51-67)	45	(37-53)
1993-97	70	(63-77)	45	(38-52)	37	(30-44)	78	(71-85)	62	(54-70)	52	(43-61)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	77	(70-84)	58	(49-67)	41	(31-51)	79	(71-87)	60	(50-70)	56	(45-67)
1988-92	81	(74-88)	64	(55-73)	50	(40-60)	79	(72-86)	69	(60-78)	59	(49-69)
1993-97	74	(67-81)	55	(46-64)	52	(42-62)	82	(75-89)	72	(63-81)	66	(56-76)

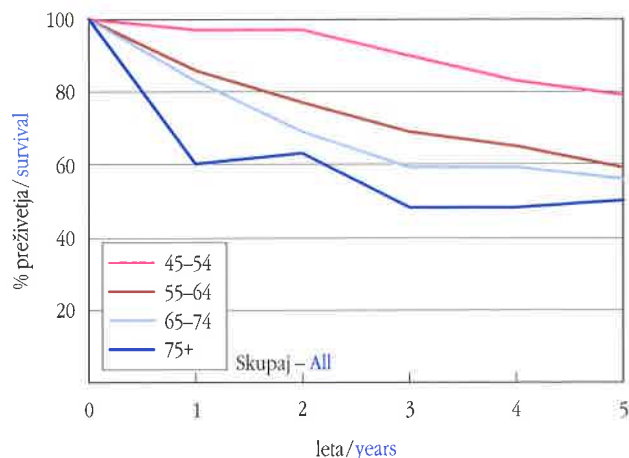
**SLIKA 2: Relativno petletno preživetje bolnikov s kronično limfocitno levkemijo, zbolelih v letih 1973-1997 po starosti in obdobju diagnoze.****FIGURE 2: Relative five-year survival of chronic lymphocytic leukemia patients diagnosed in the period 1973-1997 by age and period of diagnosis.**

V starosti 45-54 let je bilo petletno preživetje za 29% večje kot pri starejših od 75 let (slika 3). V vseh treh opazovanih obdobjih je bilo pri ženskah preživetje večje kot pri moških.

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje bolnikov s KLL pri moških 64,8% (62,1-67,6) in pri ženskah 69,2% (66,5-72), v Sloveniji pa pri moških 43,9% (36-53,5) in pri ženskah 58% (49,1-68,5). Največje preživetje pri moških je bilo 82,2% v Španiji v provincah: Baskija, Mallorca, Navarra in Tarragona in pri ženskah 85,2% v Franciji v okrožjih Bas-Rhin, Calvados in Cote d'Or.

Barbara Jezeršek Novakovič, Onkološki inštitut Ljubljana

Naraščanja incidence KLL na osnovi doslej znanih podatkov ne moremo zadovoljivo pojasniti, kajti etiologija ostaja nez-

**SLIKA 3: Relativno petletno preživetje bolnikov s kronično limfocitno levkemijo, zbolelih v letih 1993-1997 po starosti.****FIGURE 3: Relative five-year survival of chronic lymphocytic leukemia patients diagnosed in the period 1993-1997 by age.**

rate of the patients with chronic lymphocytic leukemia was 64.8% (62.1-67.6) in male patients and in female patients 69.2% (66.5-72), while in Slovenia, it was 43.9% (36-53.5) in male patients and 58% (49.1-68.5) in female patients. The highest rates of 82.2% in male patients and of 85.2% in female patients were observed in Spain (only regions: Basque Country, Mallorca, Navarra and Tarragona) and in three regions in France: Bas-Rhin, Calvados and Cote d'Or, respectively.

Barbara Jezeršek Novakovič, Institute of Oncology Ljubljana

The increase in incidence of chronic lymphocytic leukemia is not explicable from the available data because the etiology of the disease remains unknown. In general, the occurrence

nana. Sicer pa pojav ne-Hodgkinovih malignih limfomov, kamor uvrščajo tudi KLL, na splošno povezujejo z nekaterimi genetskimi boleznimi, dejavniki iz okolja in infektivnimi agensi.

Spremenjeno starostno porazdelitev v analizo zajetih bolnikov, predvsem pomik v višje starosti, lahko razložimo z boljšo diagnostično obdelavo starostnikov in posledično večjo možnostjo za odkritje bolezni v tej populaciji.

Glede terapevtskega pristopa k bolnikom s KLL še vedno velja pravilo opazovanja, dokler je bolezen stabilna. Kasneje ob napredovanju bolezni zdravimo stopenjsko: sprva z neagresivno monokemoterapijo, v primeru neuspeha pa z agresivnejšo polikemoterapijo. Novost v zdravljenju je predvsem uporaba fludarabina (v monoterapiji ali kombinacijah), s katero dosežemo večje število objektivnih odgovorov. Kljub boljšemu odzivu pa se z uporabo fludarabina celotno preživetje ni izboljšalo. Boljše relativno preživetje v zadnjih letih lahko v večji meri pripisujemo le izboljšanemu podpornemu zdravljenju (1, 2, 3, 4).

Tudi uporaba kladribina, pentostatina ter monoklonalnih protiteles v tem obdobju na preživetje bolnikov ni imela vpliva.

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of non-Hodgkin malignant lymphomas, which include also chronic lymphocytic leukemia, is related to certain genetic diseases, environmental factors, and infectious agents.

The changes in age distribution of the patients included into the analysis, particularly a shift towards older age, may be explained by the improvements in the diagnostic processing of elderly patients, thereby increasing the chances for the detection of the disease in this population.

Concerning the therapeutic approach to the patients with chronic lymphocytic leukemia, the rule of the thumb is follow-up in the period in which the disease seems to be in remission. Later on, when the disease progresses, the treatment is following a step-by-step approach: first we start with non-aggressive monochemotherapy; if it fails, we apply instead a more aggressive polychemotherapy. The most recent therapeutic improvement is the application of fludarabine as monotherapy or in combinations; its application helps to obtain a higher number of objective treatment responses, but has not had any influence upon the overall survival, which has not improved. Better relative survival in the recent years is attributable to more efficient supportive treatment (1, 2, 3, 4).

In this observation period, the use of cladribine, pentostatine and monoclonal antibodies did not have any effect on the survival.

KRONIČNA MIELOIČNA LEVKEMIJA

CHRONIC MYELOID LEUKEMIA

MKB 8 / ICD 8: 2051, 2061

V obdobju 1983–97 je zbolelo za kronično mieloično levkemijo 181 moških in 167 žensk, od tega v letih 1993–97 55 moških in 54 žensk. V analizo nista bila vključena 2 bolnika, ker je bila pri njiju levkemija ugotovljena šele ob smrti.

V opazovanem 15-letnem obdobju je bila incidenca kronične mieloične levkemije ustaljena. V letih 1983–87 je bila groba incidenčna stopnja 1,3/100.000 moških in 1,2/100.000 žensk, v letih 1993–97 pa 1,1/100.000 moških in 1,1/100.000 žensk.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V letih 1993–97 je bilo več bolnikov, starejših od 55 let.

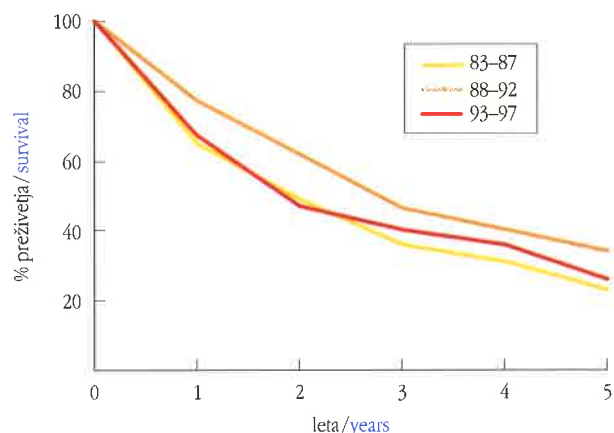
V letih 1993–97 so v 34% pričeli s prvim zdravljenjem na Kliničnem oddelku za hematologijo KC v Ljubljani, po 17% v SB v Mariboru in v Celju, po 10% v SB Šempetru pri Novi Gorici in po Slovenj Gradcu. Po en bolnik je bil zdravljen v SB v Murski Soboti, na Ptuj in v Bolnišnici Golnik. Na Onkološkem inštitutu v Ljubljani sta bila zdravljena 2 bolnika.

V opazovanem obdobju je bilo relativno petletno preživetje največje v letih 1988–92 (slika 1). Zaradi majhnega števila primerov razlike v preživetju glede na starost težko ocenjujemo. Daljše opazovanje in opazovanje v letih 1993–97 kaže, da je

TABELA 1: Kronična mieloična levkemija. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Chronic myeloid leukemia. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
		-14	15-44	45-54	55-64	65-74	75+
Males							
1983-87	64	1	15	12	6	17	13
1988-92	63	2	18	6	16	9	12
1993-97	53	0	12	8	13	9	11
Females							
1983-87	58	0	10	5	17	8	18
1988-92	54	1	10	15	9	11	8
1993-97	54	0	9	5	12	16	12



SLIKA 1: Relativno petletno preživetje bolnikov s kronično mieloično levkemijo, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of chronic myeloid leukemia patients diagnosed in the period 1983–1997 by period of diagnosis.

In the period 1983–97, a total of 181 male and 167 female patients were diagnosed with chronic myeloid leukemia; of these, 55 males and 54 females were diagnosed in the period 1993–97. In 2 patients, chronic myeloid leukemia was diagnosed at death; these patients were therefore not included in the analysis.

In the observed 15-year period, the incidence of chronic myeloid leukemia was steady. In the period 1983–87, the crude incidence rate was 1.3/100,000 in males and 1.2/100,000 in females, whereas in 1993–97, it was 1.1/100,000 in males and 1.1/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In the observation period 1993–97, more chronic myeloid leukemia cases were detected in the patients older than 55 years.

In the period 1993–97, primary treatment was started at the Department of Haematology, UMC in Ljubljana in 34%, in 17% of patients in each of General Hospitals in Maribor and in Celje, in 10% in each of General Hospitals in Šempeter pri Novi Gorici and in Slovenj Gradec. One patient was admitted to primary treatment in each of the General Hospitals in Murska Sobota, Ptuj, and Golnik, and 2 patients to the Institute of Oncology, Ljubljana.

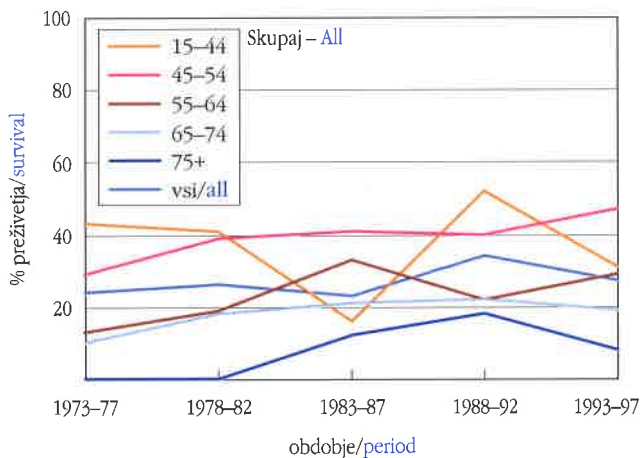
In the observation period, the relative five-year survival rate was the highest in the years 1988–92 (Figure 1). Due to a small number of cases, it is not possible to evaluate the survival rate in relation to the age distribution. From the data of a longer observation period and of the observation period 1993–97 it is evident that the survival was the highest in the patients of the age group of 45–54 years and the lowest in the patients over 75 years (Figures 2, 3).

According to the EURO CARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with chronic myeloid leukemia was 28.3% (24.5–32.7) in male patients and in female patients 35.3% (31.4–39.6), while in Slovenia, it was 15.7% (6–41.2) in male patients and 33% (19.8–55) in female patients. The highest rates

TABELA 3: Kronična mieloična levkemija. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95% intervalom zaupanja (IZ).**TABLE 3: Chronic myeloid leukemia. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).**

Obdobje/ Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	62	(50-74)	30	(18-42)	17	(7-27)	63	(50-76)	35	(22-48)	21	(10-32)
1988-92	74	(63-85)	37	(25-49)	24	(13-35)	76	(64-88)	48	(34-62)	35	(22-48)
1993-97	66	(53-79)	28	(16-40)	16	(6-26)	63	(51-75)	44	(30-58)	28	(16-40)

Obdobje/ Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	65	(52-78)	34	(21-47)	21	(9-33)	66	(53-79)	40	(26-54)	26	(13-39)
1988-92	77	(66-88)	42	(28-56)	29	(16-42)	78	(66-90)	51	(36-66)	39	(24-54)
1993-97	69	(55-83)	32	(18-46)	20	(7-33)	65	(51-79)	48	(33-63)	33	(18-48)

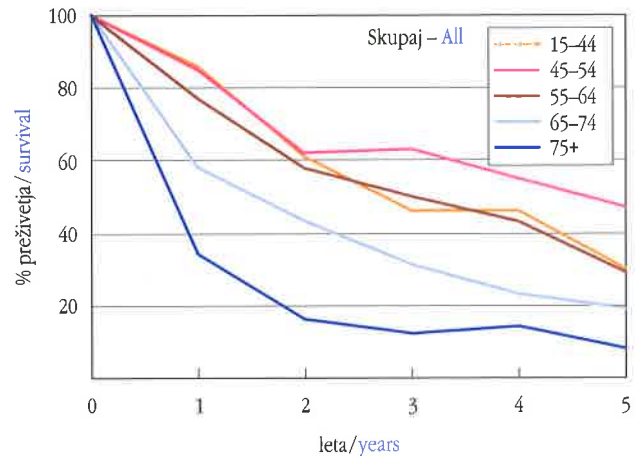
**SLIKA 2: Relativno petletno preživetje bolnikov kronično mieloično levkemijo, zbolelih v letih 1973-1997 po starosti in obdobju diagnoze.****FIGURE 2: Relative five-year survival of chronic myeloid leukemia patients diagnosed in the period 1973-1997 by age and period of diagnosis.**

preživetje največje v starosti 45-54 let in najmanjše pri starih 75 let in več (slika 2, slika 3).

Izsledki študije EURO-CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje bolnikov s kronično mieloično levkemijo pri moških 28,3% (24,5-32,7) in pri ženskah 35,3% (31,4-39,6), v Sloveniji pa pri moških 15,7% (6-41,2) in pri ženskah 33% (19,8-55). Največje preživetje pri moških in pri ženskah je bilo v Franciji v okrožjih Bas-Rhin, Calvados in Cote d'Or: 37,8% oziroma 49,1%.

Jože Pretnar, Klinični oddelek za hematologijo KC

Podatek o tem, da se v zadnjih petih letih preživetje ni izboljšalo, oziroma se je celo nekoliko poslabšalo, je presenet-

**SLIKA 3: Relativno petletno preživetje bolnikov s kronično mieloično levkemijo, zbolelih v letih 1993-1997 po starosti.****FIGURE 3: Relative five-year survival of chronic myeloid leukemia patients diagnosed in the period 1983-1997 by age.**

of 37.8% and of 49.1% in respectively male and in female patients were observed in three regions in France: Bas-Rhin, Calvados and Cote d'Or.

Jože Pretnar, Department of Haematology, UMC, Ljubljana.

The data showing that, in the last five years, the survival has not improved but rather declined is truly most surprising (1). In this period, the treatment with alpha-interferon was introduced and we also started with the program of allogenic bone-marrow transplantation.

In the period 1989-2000, we performed 22 allogenic bone-marrow transplantations. The 10-year survival or disease-free interval is expected to be 70%. This treatment modality was

ljiv (1). V tem obdobju smo pričeli zdravljenje z interferonom alfa in začeli s programom alogenične presaditve kostnega mozga.

V obdobju od 1989 do 2000 smo opravili 22 alogeničnih presaditev kostnega mozga – pričakovano 10 letno preživetje oziroma prosti interval brez bolezni je okrog 70%. To zdravljenje smo izvajali praviloma pri bolnikih, starih do 55 let. Očitno majhno število presaditev kostnega mozga ni vplivalo na celotno preživetje vseh bolnikov.

applied in the patients aged less than 55 years. Such a low number of bone marrow transplantations apparently did not have any influence on the overall survival of all patients.

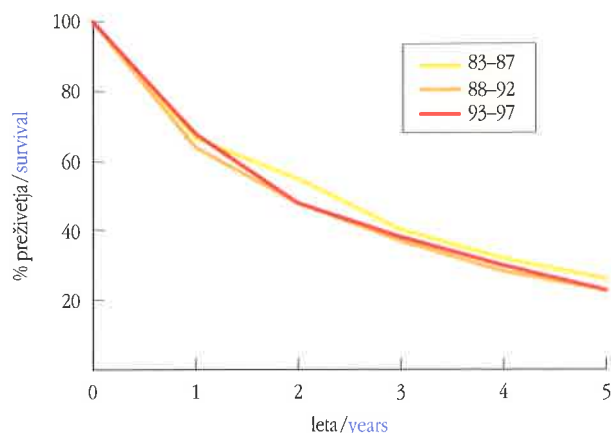
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1. Pretnar J. Allogeneic BMT for acute leukemia and chronic granulocytic leukemia in University Medical Centre Ljubljana – Slovenia. Bone Marrow Transplant 1998; 22: suppl 4: S71–2.

MULTIPLI MIELOM

MULTIPLE MYELOMA

MKB 8/ICD 8: 203



SLIKA 1: Relativno petletno preživetje bolnikov z multiplim mielomom, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of multiple myeloma patients diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za multiplim mielomom 368 moških in 430 žensk, od tega v letih 1993–97 141 moških in 172 žensk. V analizo ni bilo vključenih 37 (5%) bolnikov, ker je bila pri njih bolezen ugotovljena šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca multiplega mieloma večala. V letih 1983–87 je bila groba incidenčna stopnja 2,1/100.000 moških in 2,2/100.000 žensk, v letih 1993–97 pa 2,9/100.000 moških in 3,3/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal s 96% v letih 1983–87 na 99% v letih 1993–97.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila (tabela 1). V zadnjih letih je bilo odkritih več bolnikov, starih 55 let in več.

V letih 1993–97 je bilo specifično zdravljenih samo 69% bolnikov. Prvo zdravljenje je bilo v največjem odstotku (51%) samo citostatsko, v 26% obsevalno in citostatsko, v 15% samo obsevalno, v 5% je bila zdravljenju dodana še imunoterapija. Pri 2% način zdravljenja ni bil sporočen. V 37% so pričeli s prvim zdravljenjem na Onkološkem inštitutu v Ljubljani, v 11% na Kliničnem oddelku za hematologijo KC v Ljubljani, v 14% v SB v Mariboru, v 13% v SB v Šempetru pri Novi Gorici, v 10% v SB v Celju, po 4% SB v Novem mestu in v SB v Murski Soboti, v 3% v SB v Slovenj Gradcu, v 2% v SB na

TABELA 1: Multipli mielom. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: Multiple myeloma. Patients included in the analysis by sex, age and period of observation.

	Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis					
			-14	15-44	45-54	55-64	65-74	75+
Moški	1983-87	95	0	4	11	29	35	16
Males	1988-92	124	0	2	12	54	31	25
	1993-97	134	0	3	13	42	41	35
Ženske	1983-87	103	0	4	10	34	33	22
Females	1988-92	150	0	5	21	31	53	40
	1993-97	155	0	3	12	45	60	35

In the period 1983–97, a total of 368 male and 430 female patients were diagnosed with multiple myeloma; of these, 141 males and 172 females were diagnosed with this cancer in the period 1993–97. In 37 patients (5%), multiple myeloma was diagnosed at death; therefore, they were not included in the analysis.

In the observed 15-year period, the incidence of multiple myeloma did not significantly change. In 1983–87, the crude incidence rate was 2.1/100,000 in males and 2.2/100,000 in females, whereas in 1993–97, it was 2.9/100,000 in males and 3.3/100,000 in females.

The age distribution of patients included into the analysis has changed (Table 1). In recent years, a higher number of multiple myeloma cases was observed in the patients over 55 years.

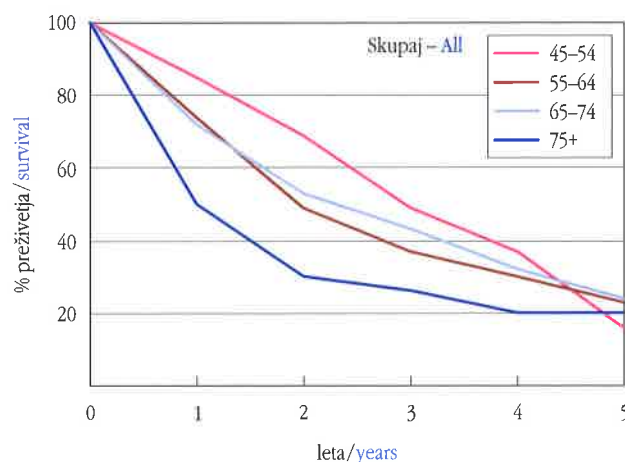
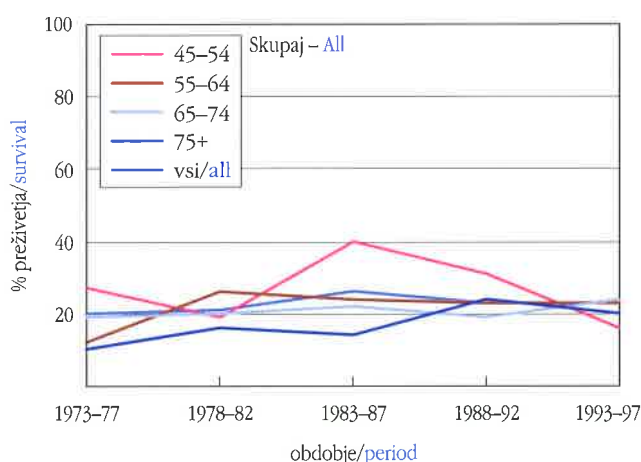
In the period 1993–97, 69% of patients underwent specific treatment. In most cases (51%), primary treatment was chemotherapy alone, 26% of patients were treated by radiotherapy and chemotherapy, 15% by radiotherapy alone and 5% received also immunotherapy. The treatment modality applied in 2% of multiple myeloma patients was not reported to the Registry. Primary treatment was started at the Institute of Oncology in 37% of patients, in 11% of patients it was started at the Department of Haematology, UMC, Ljubljana, in 14% in the General Hospital in Maribor, in 13% in the General Hospital in Šempeter pri Novi Gorici, in 10% in the General Hospital in Celje, in 4% in each of the General Hospitals in Novo mesto and Murska Sobota, in 3% in the General Hospital in Slovenj Gradec, and in 2% in the General Hospital in Ptuj. Some individual patients were admitted to primary treatment in General Hospitals in Jesenice, Izola and Trbovlje.

The relative five-year survival rate was 3% lower in the years 1993–97 than in the years 1983–87 (Figure 1) and was similar to that in the observation period 1973–82 (Figure 2). In the observation period 1993–97, the survival of female patients was worse than that in men (Table 3). The differences in survival by the age groups are significant only within the period of four

TABELA 3: Multipli mielom. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: Multiple myeloma. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje/ Period	Opazovano/Observed (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	59	(49-69)	33	(23-43)	17	(9-25)	70	(61-79)	37	(31-51)	24	(16-32)
1988-92	54	(45-63)	29	(21-37)	15	(9-21)	68	(60-76)	37	(29-45)	22	(15-29)
1993-97	65	(57-73)	39	(31-47)	18	(11-25)	66	(60-76)	30	(23-37)	18	(12-24)

Obdobje/ Period	Relativno/Relative (%)											
	Moški/Males Leta/Years						Ženske/Females Leta/Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	62	(51-73)	38	(27-49)	22	(12-32)	72	(63-81)	41	(31-51)	29	(19-39)
1988-92	56	(47-65)	33	(24-42)	19	(11-27)	70	(62-78)	41	(32-50)	26	(18-34)
1993-97	68	(59-77)	46	(36-56)	25	(16-34)	68	(60-76)	33	(25-41)	21	(14-28)



SLIKA 2: Relativno petletno preživetje bolnikov z multiplom mielomom, zbolelih v letih 1973–1997 po starosti in obdobju diagnoze.

SLIKA 3: Relativno petletno preživetje bolnikov z multiplom mielomom, zbolelih v letih 1993–1997 po starosti.

FIGURE 2: Relative five-year survival of multiple myeloma patients diagnosed in the period 1973–1997 by age and period of diagnosis.

FIGURE 3: Relative five-year survival of multiple myeloma patients diagnosed in the period 1993–1997 by age.

Ptjuju. Posamezni bolniki so pričeli z zdravljenjem še v SB Jesenice, Izola in Trbovlje.

years after the diagnosis, while in the fifth year after the diagnosis, these differences are not significant any more (Figure 3).

V letih 1993–97 je bilo relativno petletno preživetje za 3% manjše kot v letih 1983–87 (slika 1) in je bilo približno enako kot v letih 1973–82 (slika 2). Preživetje je bilo v letih 1993–97 pri ženskah manjše kot pri moških (tabela 3). Glede na starost se preživetje razlikuje vse do štirih let po diagnozi, pet let po diagnozi pa med starostnimi skupinami ni pomembnih razlik (slika 3).

According to the EURO CARE-3 study results for the period 1990–94 in Europe, the age-standardized relative survival rate of the patients with multiple myeloma was 29.6% (27.7–31.7) in male patients and in female patients 34.6% (32.7–36.6), while in Slovenia, it was 20.2% (13.1–31.2) in male patients and 21.3% (15.2–29.8) in female patients. The highest rates of 47% in male and of 49.8% in female patients were observed in three regions in France: Bas-Rhin, Calvados and Cote d'Or.

Izsledki študije EURO CARE-3 kažejo, da je bilo v Evropi povprečno starostno standardizirano relativno petletno preživetje bolnikov z multiplom mielomom pri moških 30,6% (28,8–32,6) in pri ženskah 34,6% (32,7–36,6), v Sloveniji pa pri moških 20,2% (13,1–31,2) in pri ženskah 21,3% (15,2–29,8). Največje preživetje pri moških in pri ženskah je bilo v Franciji v okrožjih Bas-Rhin, Calvados in Cote d'Or: 47% oziroma 49,8%.

Radka Tomšič, Institute of Oncology Ljubljana

Multiple myeloma is hardly ever detected in localized stage, e.g. as solitary medullary or extramedullary plasmacytoma. The

Radka Tomšič, Onkološki inštitut Ljubljana

Multipli mielom je praviloma diseminirana bolezen, le redko se pojavlja kod lokalizirana oblika – solitarni medularni in ekstramedularni plazmocitom. Slednji obliki zdravimo z observanjem, razširjen mielom pa s citostatiki. Z njimi zmanjšamo simptome, podaljšamo preživetje, ozdravitve pa običajno ne dosežemo. Vrsto let je bilo standardno zdravljenje kombinacija z melfalanom in kortikosteroidi (mediano preživetje 2–3 leta, 5 letno preživetje pa 20–30%, odvisno od razvojne stopnje bolezni, starosti, prognostičnih faktorjev, odziva na zdravljenje). Tudi novejša kombinacije citostatikov VAD in podobne sheme, kakor tudi vzdrževalno zdravljenje z interferonom, niso bistveno izboljšale preživetja.

Če primerjamo naše podatke z izsledki iz literature, so ti v grobem primerljivi in zato tudi ne preseneča dejstvo, da je petletno preživetje v opazovanem obdobju v glavnem enako (1, 2).

Ugodnejša je prognoza pri solitarnem medularnem in ekstramedularnem plazmocitomu. Daljše preživetje pa imajo tudi bolniki z začetno razvojno stopnjo in mlajši bolniki (intenzivnejša terapija).

Danes se pri bolnikih mlajših od 65 let (vendar je teh le približno polovica vseh bolnikov) odločamo za zdravljenje z visokodozno terapijo in presaditvijo avtolognih perifernih krvotvornih matičnih celic (3). To zdravljenje po raziskavah v tujini bistveno podaljša preživetje. Tega zdravljenja je bilo deležno do leta 1997 še zelo malo bolnikov, tako kakor tudi podpornega zdravljenja z bifosfonati.

Jože Pretnar, Klinični oddelek za hematologijo KC

Dejstvo, da se preživetje v zadnjem obdobju ni bistveno izboljšalo, je nepričakovano, saj zadnjih 10 let uporabljamo vrsto zdravljenj, ki bistveno podaljšajo preživetje – »VAD like« kemoterapijo. Poleg tega od leta 1996 izvajamo pri bolnikih do 60. leta starosti presaditev avtolognih perifernih krvotvornih matičnih celic, ki po raziskavah v tujini bistveno podaljša preživetje bolnikov. Relativno majhno število presaditev avtolognih perifernih krvotvornih matičnih celic v obdobju opazovanja ni vplivalo na preživetje vseh bolnikov (3).

VIRI

1. The Myeloma Trialists' Collaborative Group: Interferon as therapy for multiple myeloma: an individual patient data overview of 24 randomized trials and 4012 patients; *Br J Haematol* 200; 113: 1020–34.
2. Combination chemotherapy versus melphalan plus prednisone as treatment for multiple myeloma: an overview of 6633 patients from 27 randomized trials. Myeloma Trialists' Collaborative Group; *J Clin Oncol* 1998; 16: 3832–42.
3. Pretnar J, Preložnik Zupan I, Zver S et al. Naše izkušnje pri zdravljenju diseminiranega plazmocitoma s presaditvijo avtolognih perifernih krvotvornih matičnih celic. *Med Razgl* 2000; 39: suppl. 5: 129–32.

latter two are usually treated by irradiation. Diffuse myeloma is treated with cytostatics in order to suppress symptoms and to prolong survival; complete remission is almost impossible to obtain. The treatment modality that has long been considered as standard treatment is a combination of melphalan and corticosteroids (median survival 2–3 years; five-year survival 20–30%). The treatment outcome depends on the stage of the disease, age of the patients, prognostic factors and treatment response. The latest combinations of cytostatics, e.g. VAD or similar schedules, together with the supportive treatment with interferon did not exceptionally improve the survival. Our results are comparable to those in the literature; it is therefore not surprising that the five-year survival rate in this observation period was rather stable (1, 2).

The prognosis of solitary medullary and extramedullary plasmacytomas seems more favorable. Better survival was observed in the patients with the disease in its initial stage and young adults (more aggressive therapy).

Today, the treatment of choice applied in the patients under 65 years (this is roughly one half of all patients) is high-dose therapy in combination with the transplantation of autologous peripheral hematopoietic stem cells (3). According to the research studies carried out abroad, this combination significantly improves the survival. Until 1997, very few patients underwent this treatment or received supportive therapy with biphosphonates.

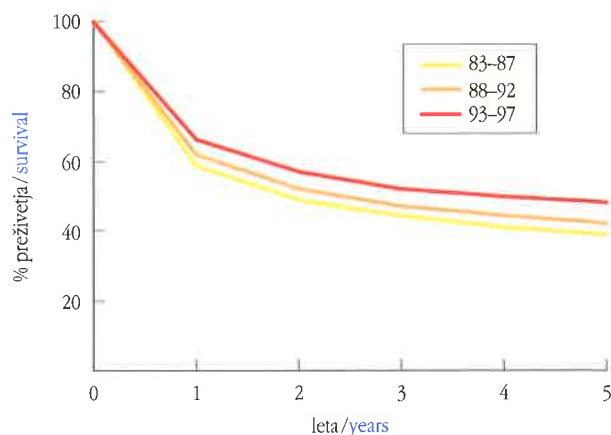
Jože Pretnar, Department of Haematology, UMC, Ljubljana

The data showing that, in the last five years, the survival has not improved are truly most surprising because, in the last decade, a series of new treatment modalities, all significantly improving the survival, were introduced, e.g. »VAD like« chemotherapy. In addition to that, since 1996, the patients under 60 years of age have been undergoing autologous peripheral hematopoietic stem cell transplantation; this is an intervention that, according to the research results obtained abroad, radically prolongs the survival. Because a relatively small number of transplantations of autologous peripheral hematopoietic stem cell were performed in this observation period they could not influence the obtained survival rate (3).

VSI RAKI, VKLJUČNO S KOŽNIM

ALL SITES, INCLUDING SKIN

MIKB 8 / ICD 8: 140–209



SLIKA 1: Relativno petletno preživetje bolnikov z vsemi raki, zbolelih v letih 1983–1997 po obdobju diagnoze.

FIGURE 1: Relative five-year survival of patients with cancers of all sites diagnosed in the period 1983–1997 by period of diagnosis.

V obdobju 1983–97 je zbolelo za rakom 50.814 moških in 48.690 žensk, od tega v letih 1993–97 19.628 moških in 19.061 žensk. V analizo ni bilo vključenih 5843 (6%) bolnikov. Pri njih je bil rak ugotovljen šele ob smrti.

V opazovanem 15-letnem obdobju se je incidenca raka večala. V letih 1983–87 je bila groba incidenčna stopnja 311,8/100.000 moških in 279,2/100.000 žensk, v letih 1993–97 pa že 407,7/100.000 moških in 372,4/100.000 žensk.

Odstotek mikroskopsko potrjenih primerov se je povečal z 89% v letih 1983–87 na 92% v letih 1993–97.

Starostna porazdelitev v analizo zajetih bolnikov se je spremenila, v zadnjih letih 1993–97 je bilo zajetih več starejših bolnikov (tabela 1). Razširjenost bolezni ob diagnozi se je ugodno spremenila le pri ženskah (tabela 2).

V letih 1993–97 je bilo specifično zdravljenih 79% bolnikov. Prvo zdravljenje je bilo v 43% samo kirurško, v 14% obsevalno, v 10% obsevalno in kirurško, v 4% samo s citostatiki, v 20% so bili citostatiki vključeni v shemo kombiniranega zdravljenja, samo s hormoni v 3%, v kombinaciji z operacijo in obsevanjem pa v 6%.

V letih 1993–97 je bilo relativno petletno preživetje za 8% večje kot v letih 1983–87 (slika 1). Preživetje se je povečalo bolj pri ženskah kot pri moških (tabela 3). Povečalo se je v vseh starostnih skupinah (slika 2). Povečanje za 8% se morda ne sli-

TABELA 1: Vsi raki. Bolniki vključeni v analizo po spolu, starosti in obdobju opazovanja.

TABLE 1: All sites. Patients included in the analysis by sex, age and period of observation.

Obdobje/ Period	Skupaj/ All	Starost ob diagnozi / Age at diagnosis						
		-14	15–44	45–54	55–64	65–74	75+	
Moški Males	1983–87 1988–92 1993–97	13472 15682 18527	151 127 124	1080 1325 1554	2216 2242 2416	3791 4942 5327	3419 3863 5893	2815 3183 3213
Ženske Females	1983–87 1988–92 1993–97	12919 14939 18122	99 102 117	1451 1809 2109	1922 2090 2502	3201 3587 3935	3084 3648 5321	3162 3703 4138

In the period 1983–97, a total of 50,814 male and 48,690 female patients were diagnosed with cancer; of these, 19,628 males and 19,061 females were diagnosed with cancer in the period 1993–97. In 5,843 patients (6%), cancer was diagnosed at death; therefore, they were not included in the analysis.

In the observed 15-year period, the cancer incidence was increasing. In 1983–87, the crude incidence rate was 311.8/100,000 in males and 279.2/100,000 in females, whereas in 1993–97, it was 407.7/100,000 in males and 372.4/100,000 in females.

In comparison to 1983–87, the increase of microscopically confirmed cases in the observation period 1993–97 was 3%, i. e. from 89% to 92%.

The age distribution of patients included into the analysis has changed. In the observation period 1993–97, more elderly patients were included into the analysis (Table 1). The stage distribution at diagnosis changed too, yet favorably only in women (Table 2).

In the period 1993–97, 79% of patients underwent specific treatment. Surgery alone was applied as primary treatment in 43% of patients, in another 14% of patients, the primary treatment was radiotherapy alone, 10% were treated by radiotherapy and surgery, 4% by chemotherapy alone, 20% underwent chemotherapy in combination with other treatment modalities.

TABELA 2: Vsi raki. Bolniki vključeni v analizo po spolu, stadiju bolezni in obdobju opazovanja.

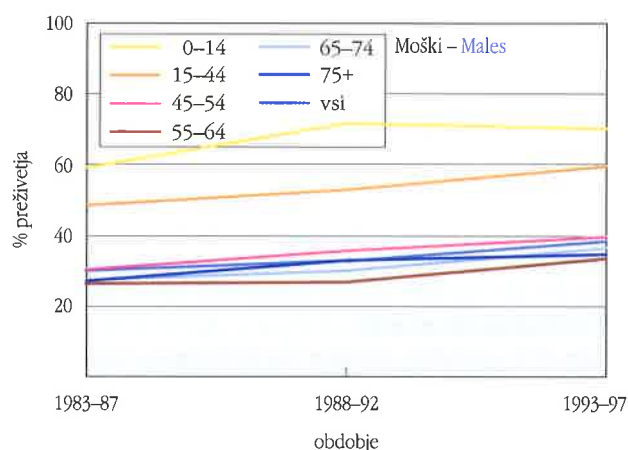
TABLE 2: All sites. Patients included in the analysis by sex, stage and period of observation.

Obdobje/ Period	Skupaj/ All	Stadij / Stage								
		Omejen/ Localized	Razširjen/ Regional	Razsejan/ Distant	Neznan/ Unknown	%				
Moški Males	1983–87 1988–92 1993–97	13472 15682 18527	4870 5510 6891	36,1 35,1 37,2	4201 4945 5789	31,2 31,5 31,2	3387 4048 4681	25,1 25,8 25,3	1014 1179 1166	7,5 7,5 6,3
Ženske Females	1983–87 1988–92 1993–97	12919 14939 18122	5184 6090 8021	40,1 40,8 44,3	3869 4473 5321	30,0 29,9 29,4	3078 3582 3936	23,8 24,0 21,7	784 794 844	6,1 5,3 4,7

TABELA 3: Vsi raki. Opazovano in relativno petletno preživetje po spolu in obdobju opazovanja s 95 % intervalom zaupanja (IZ).
TABLE 3: All sites. Observed and relative five-year survival by sex and period of observation with 95% confidence interval (CI).

Obdobje / Period	Opazovano / Observed (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	49	(48-50)	30	(29-31)	24	(23-25)	65	(64-66)	48	(47-49)	40	(39-41)
1988-92	52	(51-53)	33	(32-34)	26	(25-27)	68	(67-69)	52	(51-53)	44	(43-45)
1993-97	56	(55-57)	38	(37-39)	31	(17-19)	71	(70-72)	56	(55-57)	48	(47-49)

Obdobje / Period	Relativno / Relative (%)											
	Moški / Males Leta / Years						Ženske / Females Leta / Years					
	1	IZ/CI	3	IZ/CI	5	IZ/CI	1	IZ/CI	3	IZ/CI	5	IZ/CI
1983-87	51	(50-52)	35	(34-36)	30	(29-31)	67	(66-68)	53	(52-54)	48	(47-49)
1988-92	54	(53-55)	38	(37-39)	33	(32-34)	70	(69-71)	57	(56-58)	52	(51-53)
1993-97	59	(58-60)	43	(42-44)	38	(37-39)	74	(73-75)	62	(61-63)	57	(56-58)



SLIKA 2: Relativno petletno preživetje bolnikov z vsemi raki, zbolelih v letih 1973-1997 po starosti in obdobju diagnoze.

ši veliko. Če pa vemo, da se za tem odstotkom skriva 1482 bolnikov, pomeni to več.

V vseh obdobjih je bilo relativno petletno preživetje najboljše pri otrocih, v zadnjem obdobju 70% pri fantih in 76% pri deklicah. Pri moških, mlajših od 45 let, je bilo za 21% večje kot pri starih 75 let in več, pri ženskah pa za 28% (slika 3).

Pri razlagi preživetja in trendov preživetja vseh bolnikov z rakom skupaj moramo upoštevati, da je odstotek preživetja odvisen od deleža posameznih rakavih bolezni glede na spol in starost. Ženske zboleajo v večji meri za prognostično ugodnejšimi raki. Na povečanje preživetja vseh bolnikov v zadnjem obdobju v primerjavi s prejšnjimi, večji delež bolnikov z neme-lanonskim kožnim rakom, ki je le v izjemnih primerih lahko vzrok smrti, ni imel večjega vpliva (1).

Verjetnost preživetja posameznega rakavega bolnika pa je odvisna od tega, za katero rakavno boleznijo je zbolel, od naravnega poteka te bolezni, od razširjenosti v času diagnoze in od vseh drugih številnih dejavnikov, ki smo jih navedli že v uvodu in v razpravljanju o posameznih rakavih boleznih.

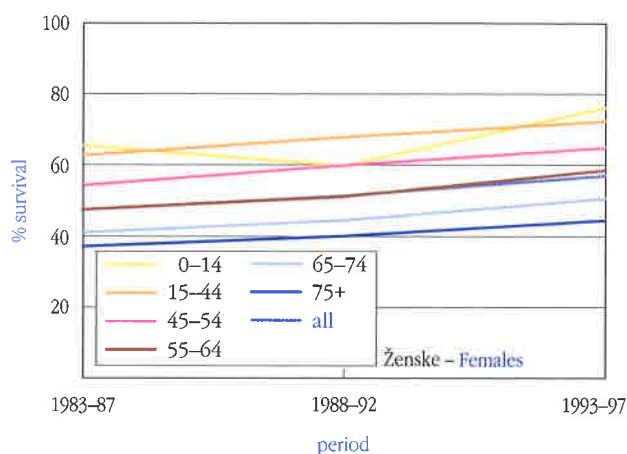


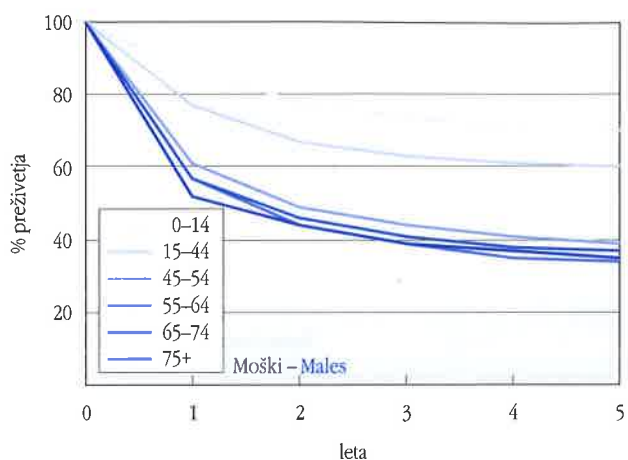
FIGURE 2: Relative five-year survival of all cancer patients diagnosed in the period 1973-1997 by age and period of diagnosis.

ties, 3% received hormonal therapy and in 6% of patients combined treatment of surgery and radiotherapy was applied.

The relative five-year survival rate was 8% higher in the years 1993-97 than in the years 1983-87 (Figure 1). The increase was higher in female patients than in male patients (Table 3). Actually, the survival improved in all age groups of patients (Figure 2). An 8-percent increase may not seem to be indicative, but it would certainly be more illustrative, if it was explicitly clear that this percentage covered 1,482 patients.

In all observation periods, the relative five-year survival rate was the highest in children; in the last observation period it was 70% and 76% in boys and girls, respectively. The survival rate in male patients below 45 years was 21% higher than in those older than 75 years, whereas in female patients, this difference was 28% (Figure 3).

The interpretation of survival and trends in survival of all cancer patients should allow for the fact that the survival rate depends on the proportion of individual cancers by sex and age. It should be noted that, in comparison to men, women



SLIKA 3: Relativno petletno preživetje vseh bolnikov z rakom, zbolelih v letih 1993–1997 po starosti.

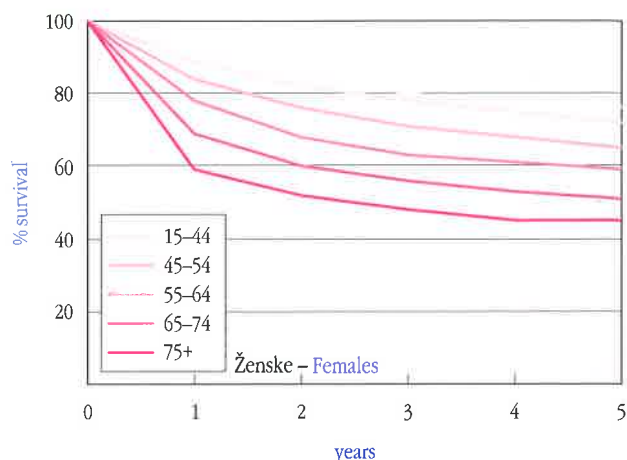


FIGURE 3: Relative five-year survival of all cancer patients diagnosed in the period 1993–1997 by age.

are affected with prognostically more favorable cancers. The improvement of survival in the recent observation period in comparison to earlier periods, can hardly be attributed to non-melanoma skin cancer that is lethal only exceptionally (1).

The probability of survival of individual cancer patient depends on the site and type of the disease, of its natural course, stage at diagnosis, and of many other factors that have been mentioned in the *Introduction* and dealt with in the discussions on individual cancer sites.

VIR

1. Pompe Kirn V, Zakotnik B, Volk N, Benulič T, Škrk J. Preživetje bolnikov z rakom v Sloveniji – Cancer patients survival in Slovenia 1963–1990. Ljubljana, Onkološki inštitut 1995.

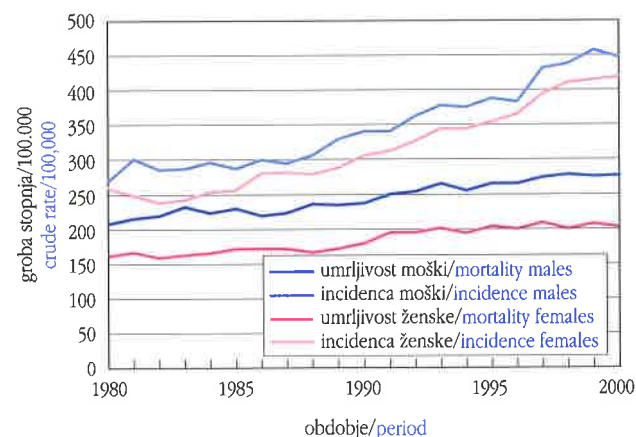
ZAKLJUČEK

Ali smo lahko zadovoljni s preživetjem bolnikov, zbolelih za rakom v letih 1983–97 v Sloveniji? Za vse bolnike z rakom, ki so zboleli v letih 1993–97, smo ugotovili, da jih je pet let po diagnozi preživel nekaj manj kot polovica (vsi v 48%, moški v 38% in ženske v 57%). Opažamo, da se preživetje izboljšuje. Zaradi večanja incidence pa število umrlih zaradi raka vsako leto še vedno narašča, vendar v zadnjem obdobju manj kot incidenca (slika 1). V obdobju 1997–2000 je bil rak kot vzrok smrti naveden povprečno letno pri 4760 umrlih (1).

Kakšne spremembe so se dogodile v Sloveniji v letih 1983–97, koliko se je povečala incidenca, za koliko se je povečalo preživetje, je bila bolezen odkrita v zgodnejšem stadiju, se je spremenila starostna struktura zbolelih, je razvidno iz prikazov in komentarjev v tej knjigi. Katera pa so tista področja, na katera bi morali biti še posebej pozorni v naslednjem obdobju, pri celostni obravnavi rakavih bolezni? Ali je to uvajanje že priznanih načinov zdravljenja, ki se pri nas zaradi različnih razlogov še niso uveljavili, ali presejanje ali primarna preventiva ali morda rak pri starejših?

Če smo v prvi knjigi zaključevali z opisom skupin rakavih bolezni glede na spremembo preživetja v obdobju 1963–87 in jih primerjali le s Škotsko in z Dansko (2), bi v tej, naši drugi knjigi, želeli v zaključku izpostaviti tiste rakave bolezni, pri katerih je neglede na ugodne spremembe v letih 1983–97 preživetje bolnikov še vedno pomembno nižje od povprečja izbranih 20 evropskih držav, vključenih v študijo EUROCORE-3 (3).

V študiji EUROCORE-3 ima Slovenija statistično značilno nižje starostno standardizirano relativno petletno preživetje od povprečja v študijo vključenih držav pri: karcinomu ustne votline, ustnega žrela, želodca, dojke, malignem melanomu, karcinomu debelega črevesa in danke, karcinomu sečnega mehurja, prostate in pri kronični limfocitni levkemiji. Pri večini drugih rakavih bolezni smo nekje med povprečjem zahodnih in vzhodnih evropskih držav.



SLIKA 1: Incidenca in umrljivost za rakom v Sloveniji po spolu, 1980–2000.

FIGURE 1: Cancer incidence and mortality in Slovenia by sex, 1980–2000.

CONCLUSION

May we possibly be satisfied with the survival of cancer patients in Slovenia in the observation period 1983–97? After the analysis of all cancer sites, we may conclude that only half of patients diagnosed in 1993–97 survived for five years from the diagnosis (all patients 48%, males 38%, females 57%). It has been observed that the survival is improving despite the fact that the mortality rate continues to increase, though in the last observation period, much less than the incidence rate (Figure 1). In the years 1997–2000, cancer was reported to be the cause of death on average in 4,760 cases per year (1).

This publication, containing the presentations of survival data and commentaries of clinicians, is an illustration of the changes that occurred in Slovenia in the years 1983–97, and are resumed in the following issues: How much did the incidence increase? How much did the survival improve? Was cancer detected in an early stage? Did the age pattern of cancer patients at diagnosis change? Which cancer sites should be paid particular attention to in the next observation period? Where should we look for the causes of poor improvement in some cancer sites? In the treatment modalities that are widely recognized as most effective, but for various reasons not yet applied in Slovenia? In lacking screening programs or primary prevention? Or in cancer in the elderly?

We concluded the first report with an outline of cancer sites from the viewpoint of the changes in survival in the period 1963–87 and compared them only with the data from Scotland and Denmark (2). In the conclusion of our second report, we would like to expose those cancers with the survival rates that are, regardless of a number of most favorable changes in the observation period 1983–97, different from the average rate obtained from 20 European countries included into EUROCORE-3 study (3).

From the EUROCORE-3 study, it is obvious that Slovenia has significantly lower age-standardized relative five-year survival rates in the carcinomas of the oral cavity, pharynx, stomach, breast, in malignant melanoma, in colorectal, bladder and prostate cancer and in chronic lymphatic leukemia than the average rates of other countries included in the study. The survival rates in other cancers are more or less close to the average rate obtained from 20 European countries included into EUROCORE-3 study (3).

Living standard is an important determinant of life expectancy as well as of the observed survival. I am therefore certain that a positive trend in five-year survival rates in three recent consecutive observation periods are more important indicators of improvement than the comparison with other European countries. The changes in survival rates are shown in Figure 1 of each chapter. It is encouraging to see that the survival is improving in the majority of malignant diseases, in some of them remarkably, in others less notably. Regrettably, this same trend has not been observed in bladder cancer, multiple myeloma, acute non-lymphoblastic leukemia, and chronic myeloid leukemia.

In this publication, the clinicians who had been for years involved in the treatment of particular cancer sites commented on the majority of reasons for poor survival in some of cancers in Slovenia that is below the European average rate and for almost no improvement in the last fifteen years. In these concluding pages, I wish to make a summary of their observations and add to them further clarification.

Življenjski standard je pomembna determinanta tako pričakovane kot opazovanega preživetja. Zato se mi zdi izboljšanje petletnega preživetja v treh zaporednih petletnih obdobjih pomembnejši kazalec kot primerjava z drugimi evropskimi državami. Te spremembe preživetja so prikazane v sliki 1 pri vsakem posameznem poglavju. Spodbudno je, da se preživetje izboljšuje pri večini rakavih bolezni (nekje bolj, drugje manj). Tega trenda pa žal ne opažamo pri naslednjih rakih: karcinomu sečnega mehurja, multiplemu mielomu, akutni nelimfoblastni levkemiji in kronični mieloični levkemiji.

Kljub temu, da so o večini razlogov, zakaj je pri naštetih rakih preživetje pod evropskim povprečjem ali zakaj se ni v zadnjih petnajstih letih izboljšalo, v tej knjigi že razpravljali kliniki, ki se s posameznimi boleznimi ukvarjajo že vrsto let, želim v naslednjih odstavkih to na kratko povzeti in dodatno pojasniti.

KARCINOM USTNE VOTLINE IN USTNEGA ŽRELA

Pri raku ustne votline (brez raka jezika) in ustnega žrela v Sloveniji statistično značilno zaostajamo za evropskim povprečjem, ki je pri raku ustne votline za moške 39,9%, pri nas pa le 21,5% in pri raku ustnega žrela za moške 25,3% pri nas pa 15,1%. Kljub temu, da je trend ozdravitve pri teh bolnikih pri nas ugoden, saj se jih pozdravi v zadnjem petletnem obdobju kar za tretjino več, je stanje še vedno slabo (slika 1, stran 16). Incidenca te socialne bolezni je v Sloveniji velika in bolniki prihajajo na zdravljenje v napredovanem stadiju. Ker presejanje ni izvedljivo, vzroki pa so dobro znani, bi bila pri reševanju problema te bolezni še najbolj smiselna primarna preventiva. Upam, da bo z novimi zakoni o kajenju in alkoholu in z večjo skrbjo za obrobne skupine prebivalcev, prišlo v slovenski družbi do pozitivnih premikov prav na področju preprečevanja. V samem izidu zdravljenja te bolezni pa pričakujem v naslednjih obdobjih še nadaljne približevanje drugim evropskim državam, saj bo večji odstotek bolnikov kot je bil v preteklosti, zdravljen kombinirano.

ŽELODČNI RAK

Kljub temu, da je incidenca želodčnega raka v rahlem upadanju, je še vedno velika saj je v letih 1993–97 zbolelo 2365 bolnikov. Le petina jih je imela ob diagnozi omejen stadij (T1, 2, N0, M0), pri katerem je odstotek s kirurgijo ozdravljenih bolnikov velik. Problem je podoben povsod v Evropi, saj je bilo povprečno petletno starostno standardizirano relativno preživetje komaj 24%. V Sloveniji je bilo slabše (15% za moške in 19% za ženske). Primerjava po stadiju z ostalimi državami, vključenimi v EUROCORE-3 ni možna, tako, da glavnega razloga za te razlike ne moremo ugotoviti. V obdobju 1990–94, ki ga EUROCORE-3 obravnava, standardov kirurgije (način operacije, operacija v ustanovi, ki obravnava večje število bolnikov) in patologije pri nas še ni bilo. Uvedeni pa so bili, kot navaja v svojem komentarju prof. dr. Repše, kmalu zatem. Tako menim, da se bomo lahko kmalu približali evropskim državam. K temu bo pripomogla tudi večja dostopnost do endoskopskih preiskav in do dopolnilnega zdravljenja tistih bolnikov, pri katerih je to indicirano (4).

CANCER OF THE ORAL CAVITY AND PHARYNX

In the survival of patients with the cancer of the oral cavity (with the tongue excluded) and pharynx, Slovenia is significantly lagging behind the European average rate. In male patients with oral cavity cancer, the rates in Europe and in Slovenia are 39.9% and only 21.5%, respectively, while in those with mesopharyngeal cancer, these rates are 25.3% and 15.1%, respectively. Though the tendency to cure seems favorable in Slovenia, as a third more patients were cured in the last observation period, the circumstances continue to be desolate. (Fig. 1, p. 16). The incidence rate of this disease with a strong social stigma is very high in Slovenia. The patients are coming for treatment when the disease is in its advanced stages. As screening is not possible and the causes of this disease are well known, the most sensible strategy to fight against this cancer is primary prevention. Hopefully, the new law, restricting the alcohol and cigarette abuse and paying more attention to the social welfare of the poorest and marginal groups of people, will bring about the changes for the better in the prevention endeavors of Slovenian people. I also honestly hope that the treatment results will get closer to those in other European countries because, in the future, a higher proportion of oral cancer patients will be receiving combined therapy.

STOMACH CANCER

Though the incidence of stomach cancer is moderately decreasing, it is nevertheless high; in the period 1993–97, 2,365 patients were diagnosed with stomach cancer. In less than one fifth of them, the disease was detected in localized stage (T1, 2, N0, M0). Localized disease is manageable by surgery, yielding the cure of a high percentage of patients. The European countries are facing a similar problem as the average five-year age-standardized relative survival is hardly reaching the rate of 24%. In Slovenia, it is even worse, hardly 16% in men and 19% in women. A comparison by stage distribution with other countries included into EUROCORE-3 is not possible. This is why we cannot provide any definite explanations for these differences. In the period 1990–94, analyzed in the EUROCORE-3 study, no surgical standards (surgical method, surgery to be performed in a health care institution that treats a greater number of stomach cancer patients) neither pathological ones were elaborated in Slovenia. According to Professor Repše's comments, such standards were introduced soon after that period. To my view, we will soon be able to catch up with other European countries' rates. Better accessibility to and availability of endoscopy and adjuvant treatment of patients eligible for it will certainly help to improve treatment results (4).

BREAST CANCER

The survival of breast cancer patients is gradually improving. According to EUROCORE-3 study, the average five-year age-standardized relative survival of breast cancer patients in Europe is 74.8%, whereas in Slovenia, it is 65.6%. The difference of almost 10% means that, in the period 1993–97, we could have avoided around 400 deaths due to breast cancer. All that we could and should have also done is summarized in the commentaries by Professor Čufer and Professor Lindtner.

RAK DOJKE

Preživetje se s časom izboljšuje. V EUROCORE-3 je povprečno petletno starostno standardizirano relativno preživetje za ženske v Evropi 74,8%, v Sloveniji pa 65,6%, skoraj 10% razlika. Ta razlika pomeni, da bi se lahko v letih 1993–97 v Sloveniji izognili približno 400 smrtim. Kaj bi še lahko storili, si lahko preberemo v komentarju prof. dr. Čuferjeve in prof. dr. Lindtnerja. Ker se pri nas v vsem obdobju opazovana razmerja med stadiji bolezni skoraj ni spremenilo (Tabela 1, stran 35), menim, da je potrebno največ moči usmeriti prav na organizirano presejanje. Zaradi več dejavnikov (ne samo finančnih!) to ne bo enostavno. Kot navaja prof. dr. Čufer, samo povečanje mamografskih centrov ni imelo prav nobene zadošča, pomembni so kakovostni izvajalci presejanja, kontrola kakovosti dela, dobro organizirana povezava med diagnostično in terapevtsko službo in seveda ozaveščene ženske. V letih 1989–1991 ozaveščenost žensk, merjena z odstotkom odzivnosti na ponujeno mamografijo, ponekod v Sloveniji še ni bila dovolj velika (v takratni občini Ljubljana-Center le 56% in Maribor-Rotovž le 53%) (5). Ponovno se bo morala zbrati skupina strokovno podkovanih in motiviranih zdravnikov ter ostalih zdravstvenih delavcev, koordiniranih s strani Onkološkega inštituta, da bo lahko izpeljala iniciativo, ki sta jo dala tako Ministrstvo za zdravje kot civilna družba (Europa donna). Dokler pa se ne bo našel nekdo, ki se bo temu delu popolnoma posvetil in poizkušal teorijo spremeniti v prakso, bo v Sloveniji še vedno vsako leto umrlo po nepotrebnem približno 100 bolnic zaradi raka dojke.

MALIGNI MELANOM

Incidenca se večja. Relativno starostno standardizirano preživetje je bilo za zbolele v letih 1990–94 daleč pod povprečjem EUROCORE-3 (Evropa: 81%, Slovenija: 65%). V zadnjem petletnem obdobju (1993–97) se je pomebno izboljšalo, vendar se je izboljšalo tudi drugod. Preživetje se izboljšuje, razlike ostajajo (6). Glavni napovedni dejavnik za preživetje je debelina primarnega tumorja. Z dodatnim zdravljenjem po operaciji preživetja zaenkrat ne moremo pomembno izboljšati. Rešitev vidim tako predvsem v dobri primarni in sekundarni preventivi. O bolezni je potrebno govoriti v javnosti, da se ljudje z njo seznanijo in gredo ob sumljivih spremembah pravočasno k zdravniku. Zdravniki pa morajo imeti ustrezno znanje za prepoznavanje in pravilno zdravljenje bolezni. Najboljši zgled za uspešne tovrstne ukrepe so nam sporočili iz Avstralije (7).

KARCINOM DEBELEGA ČREVEŠA IN DANKE

V obdobju 1985–89 je bilo v ZDA petletno relativno preživetje bolnikov s karcinomom debelega črevesa in danke statistično značilno boljše kot v Evropi (debelo črevo: ZDA 60%, Evropa 48%, Slovenija 36%, danke: ZDA 57%, Evropa 44%, Slovenija 30%) (8, 9, 10, 11). Ko so analizirali, zakaj takšna razlika, so prišli do zaključka, da sta glavni vzrok boljšemu

As in Slovenia, the stage distribution did not change throughout the observation period, (Table 1, p. 35), I am confident that most of our endeavors should from now on focus on the development and implementation of screening program although, for several reasons (not solely financial) it will not be simple at all. As noted by Professor Čufer, the mere propagation of mammography in Slovenia did not have any favorable impact on earlier diagnosis of breast cancer. It is obvious that technical equipment alone does not provide the desired results; in fact, more important are well-trained experts in screening, quality control, appropriate and close cooperation between diagnostic and therapy departments, and above all, highly conscientious women. In a pilot study in 1989–1991 in three regions of Slovenia, we offered women free screening mammography and physical examination; but the compliance rate in some communities was low (in Ljubljana-Center only 56%, and in Maribor-Rotovž only 53%) (5). Again, we will have to set up a group of experts gathering experienced and highly motivated medical doctors and other health care professionals and coordinate its activities in order to implement the incentive given by the Ministry of Health and non-governmental organization «Europa Donna». As long as we do not find a person who could be wholly in charge of and committed to these activities and goals, as well as capable of turning theory into practice, around 100 breast cancer patients will unnecessarily die of this cancer yearly.

MALIGNANT MELANOMA

Malignant melanoma incidence has been increasing. The 1990–94 survival rate was far below the EUROCORE-3 average rate (Europe 81% vs. Slovenia 65%). In the recent observation period 1993–97, a significant improvement was observed in Slovenia; but, it happened also elsewhere. The survival rates are improving, but «the differences remain wide» (6). One of the major prognostic factors for survival is primary tumor thickness. So far, adjuvant postoperative treatment has not proved to be as effective as to improve significantly the survival. The best solution would be a well-designed primary and secondary prevention. We should speak a lot about this disease in public in order to keep people attentive to suspicious changes and advise them to consult the doctor in time. On the other hand, medical doctors should have adequate knowledge and experience to identify the disease and treat it properly. To date, the most promising reports about successful preventive measures have been received from Australia (7).

COLORECTAL CANCER

In the period 1985–89, the five-year survival of colorectal cancer patients in USA was significantly more favorable than in significantly Europe (colon: USA 60%, Europe 48%, Slovenia 36%; rectum: USA 57%, Europe 44%, Slovenia 30%) (8, 9, 10, 11). After analyzing these differences, it was concluded that better survival in USA is largely due to lower disease stage at diagnosis and to a more favorable histologic type. The disease stage remains one of the major prognostic factors for the survival if the cancer is properly treated. And the major difference between colorectal cancer patients in Slovenia and those in Northern and Western Europe is precisely the disease stage (10).

preživetju v ZDA nižji stadiji ob ugotovitvi diagnoze in ugodnejša histološka vrsta. Stadij je ob primernem zdravljenju glavni napovedni dejavnik preživetja. Razlika med nami in severno ter zahodno Evropo je predvsem v stadiju bolezni (10).

Vzpodbudno je, da se je v zadnjem opazovanem obdobju tudi v Sloveniji preživetje izboljšalo. Težko je zaključiti, ali zaradi tega, ker je več omejenega stadija (manj verjetno, če primerjamo številke), ali zaradi boljšega terapevtskega pristopa (12). V začetku 90. let smo v Sloveniji pričeli uvajati povsem drugačen pristop pri zdravljenju bolnikov z rakom debelega črevesa. Ta pristop se v naši analizi za leta 1993–97 še ne kaže v celoti, saj je bil v tem obdobju zdravljen le manjši delež bolnikov po principih kot jih opisuje v komentarju prof. Repše. Ali se bomo z uvedbo takšnega zdravljenja pri večini bolnikov približali evropskemu (kaj šele ameriškemu) povprečju, bodo pokazale bodoče analize. Verjetno pa to ne bo dovolj, ker bo stadij še vedno ostal glavni napovedni dejavnik za preživetje.

Pri raku debelega črevesa sem optimist, saj upam, da se bomo z zastavljenimi standardi, z boljšo informiranostjo prebivalcev, boljšim dostopom do modernih diagnostičnih metod, z njihovo racionalno uporabo in uvajanjem novosti v zdravljenju kmalu približali zahodni Evropi.

Pri karcinomu danke, kjer glede preživetja še bolj zaostajamo za evropskim povprečjem, je stvar bolj zapletena, saj so se standardi, ki smo jih uvajali v začetku 90. let spremenili. To velja tako za področje kirurgije (nove tehnike operacije) kot radioterapije, ki sta poleg stadija glavna napovedna dejavnika preživetja. Morda bi bilo pri raku danke smiselno po vzoru iz preteklosti (13) ponovno zastaviti raziskavo ali pa se priključiti kakšni dobro zastavljeni mednarodni raziskavi in se na ta način kar najhitreje približati evropskemu povprečju.

Ker je pri večini bolnikov z rakom debelega črevesa in danke ob diagnozi stadij že napredovan in preživetje slabo, je potrebno na osnovi novih spoznanj tudi v Sloveniji razmišljati o organiziranem presejanju teh dveh bolezni.

RAK PROSTATE

Preživetje bolnikov z rakom prostate v Sloveniji statistično značilno zaostaja za povprečjem v študijo EURO CARE-3 zajetih držav (Evropa: 61,5%, Slovenija 47,3%). Razlog je verjetno zelo kompleksen, vreden natančne analize. Po podatkih o pričetku prvega zdravljenja lahko sklepamo, da so se skoraj vsi bolniki v Sloveniji pričeli zdraviti v regiji, kjer stanujejo. V onkologiji naj bi veljalo načelo, da prvo zdravljenje maligne bolezni načrtuje multidisciplinarni konzilij. Bojim se, da je le majhen odstotek bolnikov z rakom prostate, v Sloveniji jih je letno več kot 400, predstavljen urološkemu konziliju, kjer naj bi bila poleg urologa prisotna tudi za raka prostate specializirana onkolog-radioterapevt in onkolog-internist. Največ »za in proti« razprav po kongresih je ravno o zdravljenju raka prostate. Kolikšno je najmanjše število bolnikov, ki bi ga moral določeni center zdraviti letno, da bi si pridobil dovolj izkušenj? Ali lahko s široko uporabo PSA kaj prispevamo k izboljšanju preživetja? Morda se stvari izboljšujejo, vendar ostaja v Sloveniji preživetje slabo. Kot ugotavlja prim. Marolt, je stanje pri nas enako kot v 80. letih.

It is however most encouraging that, in the last observation period, the survival improved also in Slovenia, though it is not easy to assess whether this improvement results from more cases of localized disease (which is, with regard to the figures, less likely) or from better therapeutic approach to colorectal cancer patients (12). In the early 1990s, a completely new treatment approach to the colon cancer patients was initiated in Slovenia, but its impact on the survival for the period 1993–97 cannot be seen yet because, in this period, only a minor proportion of colon cancer patients were treated according to the standards as described by Prof. Repše. Whether or not this most recent treatment modality will bring us closer to the European average rate (let alone the American one) will be readily demonstrable only by future analyses. We may expect that this new approach alone will not be sufficient because the disease stage will continue to be the most important prognostic factor for survival.

I allow myself to be optimistic about the colon cancer as there is hope for Slovenia to meet the West-European average rates by setting up new standards, higher awareness of people in general, easier availability and sensible application of up-to-date diagnostic methods and introducing of innovations into our practice.

In the survival of rectal cancer patients, we are considerably lagging behind the European average rate because the situation is rather more complex since the standards that were introduced in the early 1990s have changed. This is as much true in surgery (new techniques!) as in radiotherapy that are both, beside the disease stage, the major prognostic factors for survival. At this point, we should look back and reconsider the possibility of drawing up a new study or to join a well-designed international study and through it reach the level of European average rate.

Since the main reason for the poor survival of patients is the advanced stage, it would be appropriate to introduce an organized screening program in Slovenia also.

PROSTATE CANCER

The survival rate of prostate cancer patients in Slovenia is statistically significantly lower than the average rates of the countries included into the EURO CARE-3 study (Europe 61.5%, Slovenia 47.3%). The reason may be complex and multifaceted, deserving a detailed analysis. From the data on primary treatment we may conclude that almost all patients received it in the district of their residence. The rule of thumb in oncology is that the primary treatment of a malignancy should be planned by multidisciplinary advisory team. In Slovenia, a total of 400 of new prostate cancer cases are detected yearly and I am concerned that a too low percentage of these patients is referred to the Multidisciplinary Advisory Team for Urology, consisting of an urologist, a radiation oncologist and a medical oncologist. At oncology congresses, the most burning 'pros and cons' debates evolve around the treatment of prostate cancer.

What would be the minimum number of prostate cancer patients treated yearly at a certain health care institution that could be a guarantee of high proficiency and skill of that institution in the prostate cancer treatment? Could we, to any extent, contribute to the improvement of survival by tumor marker tests

RAK SEČNEGA MEHURJA

Pri raku sečnega mehurja težko ugotavljamo, kje je naše mesto v Evropi, saj eni registri vključujejo intraepitelijski površinski rak mehurja, drugi ne. Iz podatkov, ki jih imamo na voljo, tako ne moremo potegniti najbolj tehtnih zaključkov. Rak sečnega mehurja izpostavljam zato, ker se preživetje v zadnjih 15. letih ni nič izboljšalo (slika 1, stran 61). Koliko bolnikov z invazivnim rakom je bilo dejansko zdravljenih z radikalno cistektomijo, ki je deklariran standardni način zdravljenja? Po podatkih Registra (možnost nepopolne prijave?) zelo malo (13%). Ob napredovanem stadiju je tudi premajhen odstotek radikalno operiranih lahko razlog za slabše preživetje. Vsekakor bo potrebno pri mišično invazivnem raku mehurja v Sloveniji izboljšati pristop, če želimo, da ne bo tudi pri naslednjem pregledu preživetje enako kot v 80. letih.

KRONIČNA LIMFOCITNA LEVKEMIJA

Povprečno petletno starostno standardizirano relativno preživetje za obdobje 1990–94 je bilo v Evropi za moške 64,8% (pri nas 43,9%) in za ženske 69,2% (pri nas 58%). Smo med državami z najslabšim preživetjem v Evropi. Incidenca v državah, kjer registri pokrivajo vso populacijo, pa je podobna tisti v Sloveniji.

V obdobju 1993–97 je bilo, po podatkih Registra, ob postavitvi diagnoze specifično zdravljenih 38% bolnikov. Razlog temu je strategija zdravljenja bolezni, ki se zdravi šele, ko postane simptomatska, delno pa nepopolna in pomanjkljiva prijava hematoloških ambulant v Sloveniji. Zakaj torej tako slabi rezultati? Ali so naši bolniki deležni slabšega zdravljenja, predvsem slabšega podpornega zdravljenja? V zdravljenje kronične limfocitne levkemije prihajajo nova, draga zdravila. Strošek bo toliko večji, če smo že s 'starimi in poceni' načini zdravljenja ozdravili manjši odstotek bolnikov kot bi ga lahko.

AKUTNE NELIMFOBLASTNE LEVKEMIJE

Preživetje bolnikov, ki zbolijo zaradi akutne nelimfoblastne levkemije, je v okvirih evropskega povprečja. S tem ne moremo biti zadovoljni, ker bi bilo lahko preživetje bolnikov pri nas med boljšimi v Evropi, če se ne bi ravno v zadnjem petletnem obdobju poslabšalo (slika 1, stran 103). Če pozorno pogledamo sliko 2, stran 104, vidimo, da se je najbolj znižalo ravno preživetje bolnikov starih 15–44 let. Nekateri od teh bolnikov so bili že v tem obdobju deležni bolj agresivnega zdravljenja (transplantacija kostnega mozga), ki se je ravno takrat pričelo uvajati tudi pri nas. Predpostavljam, da so rezultati slabši ravno zaradi obdobja uvajanja in da bodo že naslednje analize pokazale občutno izboljšanje preživetja teh bolnikov.

KRONIČNA MIELOIČNA LEVKEMIJA

Podobno kot za akutno mieloično levkemijo velja verjetno tudi za kronično mieloično levkemijo (sliki 1 in 2, stran 109

for PSA? It may seem that the treatment potentials are changing for better; nonetheless, the survival continues to be poor. As noticed by Dr. Marolt of the Institute of Oncology Ljubljana, the situation is currently the same as it was in the 1980s.

BLADDER CANCER

With respect to bladder cancer, we cannot make a straightforward estimation where Slovenia ranks in Europe because some registries in Europe include superficial bladder tumors into the analysis of bladder cancer while others do not. From the available data, we can hardly draw any reliable conclusion. I would like to highlight particularly the bladder cancer because the survival rate in both sexes has not improved in the last 15 years (Figure 1, p. 61). How many patients with the invasive bladder cancer were actually treated by radical cystectomy that is considered as standard treatment modality? According to the data from the Registry, this number is rather low, only 13% (possibly due to incomplete notification). Among the patients with the disease in more advanced stages, the percentage of those who underwent radical surgery is too low. This may also be one of the reasons for poorer survival. It is obvious that we will have to make some improvements in the treatment approach to the muscle invasive bladder cancer if, in the next observation period, we hope for the survival that would not match up with that in the 1980s.

CHRONIC LYMPHOCYTIC LEUKEMIA

In the years 1990–94, the average European five-year age-standardized relative survival rate of male patients with chronic lymphocytic leukemia was 64.8% (in Slovenia 43.9%) and of female patients 69.2% (in Slovenia 58%). The survival rate in Slovenia is among the lowest in European countries. The incidence in the countries with the cancer registries covering the whole country is similar to the incidence in Slovenia.

The Registry data support that, in the period 1993–97, 38% patients received specific treatment at diagnosis. This low percentage may be due to the treatment strategy: this disease is often treated only after it is confirmed to be symptomatic, and partly also due to incomplete notification of the cases by hematology departments at various health care institutions in Slovenia. Why then such poor results? Are the patients in Slovenia receiving less effective therapies, in particular less effective supportive treatment? At present, new and expensive drugs are being developed and will soon be introduced into clinical practice. The costs of treatment of patients with chronic lymphocytic leukemia with new drugs will be much higher accordingly.

ACUTE NON-LYMPHOBLASTIC LEUKEMIAS

In Slovenia, the survival of patients with acute non-lymphoblastic leukemia is within the average European rates. Though favorable, this comparison is far from being soothing because, in Slovenia, the survival of these patients could have been among the highest in Europe if it had not declined in the last five-year observation period (Fig. 1, p. 103). A closer look

in 110). Posebno zanimiva bo analiza za naslednje obdobje, ko se bo, upam, pokazal učinek imatinib mesilata, novega zdravila za kronično mieloično levkemijo.

MULTIPLI MIELOM

Kljub novim, bolj učinkovitim zdravilom in boljšemu podpor-nemu zdravljenju je bilo preživetje v letih 1983–97 skoraj enako (slika 1, stran 115). Morda pri multiplem mielomu bolj intenzivno zdravljenje ne pomeni tudi boljše zdravljenje?

RAK PRI STAREJŠIH

Posebej bi želel opozoriti še na problem zdravljenja in pre-živetja starejših bolnikov z rakom. V letih 1993–97 je bilo v Slo-veniji 34% bolnikov ob diagnozi raka starih 70 let ali več. Kot je razvidno iz prikazov o preživetju po starostnih skupinah je pri teh bolnikih preživetje v primerjavi z mlajšimi slabo. Sama starost v našem prikazu ni vplivala na razliko. Relativno pre-živetje namreč upošteva pričakovano trajanje življenja glede na starost.

Na problem starejših bolnikov z rakom opozarjajo tudi drugod po svetu in mu v zadnjem času posvečajo tudi več pozor-nosti (14). Razlogov za to je več. Standardno zdravljenje za posamezno rakavo bolezen je lahko kontraindicirano zaradi spremljajočih bolezni; včasih pa je to le naš predsodek zara-di same koledarske starosti bolnika. Vsa standardna zdravlje-nja, ki so se izkazala za učinkovita v kliničnih raziskavah, pa verjetno ne veljajo za starejše bolnike. Ponavadi je bil in je še vedno eden od izključitvenih kriterijev za vstop v klinično razi-skavo prav starost (npr. starejši od 70 let).

Priporočajo, da se morajo zdravniki posebej usposobiti za zdrav-ljenje raka pri starejših bolnikih, saj to zahteva še dodatna zna-nja in drugačen pristop (15, 16, 17, 18).

at Figure 2 (p. 104) reveals that this decline was the biggest in the age group of patients of 15–44 years. Some of these patients underwent more aggressive therapies (e. g. bone mar-row transplantation) that were being initiated into the clinical practice in Slovenia right in that observation period. I presume that poorer treatment results could be attributed to the initia-tion phase of the new method and that all the subsequent analy-ses will show an improvement in the survival of our patients.

CHRONIC MYELOID LEUKEMIA

A similar assessment as that for acute myeloid leukemia can be made also for chronic myeloid leukemia (Figs 1 and 2, p. p. 109 and 110). The analysis of the next observation peri-od, in which the impact of a new drug for chronic myeloid leukemia (imatinib mesilata), will have been felt already, will hopefully show some progress in the survival of our patients.

MULTIPLE MYELOMA

Despite new more effective drugs and improved supportive treatment the survival in the years 1983–97 was more or less steady (Fig. 1, p. 115). We are still not sure whether a more aggressive therapy applied for multiple myeloma is also more effective therapy.

CANCER IN THE ELDERLY

I would like to draw the reader's attention to the treatment and survival of elderly cancer patients, which present a par-ticular challenge to oncologists. In the period 1993–97, 34% of all newly detected cancer patients were older than 70 years. The graphs showing the survival by age groups indicate clearly that the survival of the elderly in comparison to that of younger patients is poorer. In our presentation, the age alone does not affect the difference in survival. In effect, the relative survival rate takes account the life expectancy with respect to the actual age.

Cancer in the elderly is a problem worldwide and has been recently given more attention than earlier (14). There are many reasons. Standard treatment of the elderly for each individ-ual cancer may sometimes be a contraindication to various accompanying diseases. Yet, sometimes, it could be only our prejudice arising from the concern for the patients due to their old age. The standard treatment modalities that proved to be very effective in clinical studies, were not always as effective in the elderly. A frequent exclusion criterion of the patients from a clinical study has been patient's age, e. g. patients aged over 70.

It has been recently recommended that oncologists should specifically specialize in the treatment of cancer in the eld-erly because this requires additional knowledge and skills as well as different approaches (15, 16, 17, 18).

Branko Zakotnik

SKLEPNE MISLI

Želja urednikov te knjige je, da bi pričujoči podatki in komentariji vzpodbudili vse zdravnike, ki se z zdravljenjem raka ukvarjajo, k še boljšemu interdisciplinarnemu delu. Verjamemo, da bi le tako lahko izboljšali preživetje bolnikov z rakom v Sloveniji.

Menimo, da je v Sloveniji rakavih bolezni, katerih incidenca je majhna, zdravljenje pa zapleteno, smiselno zdraviti na enem mestu (npr. maligne limfome, sarkome, raka ščitnice, germinalne tumorje). Za bolezni, ki jih je veliko (npr. raka dojk, raka debelega črevesa in danke, pljučnega raka), je potrebno zdravljenje v nekaj centrih. Ti centri pa morajo obravnavati dovolj veliko število bolnikov in slediti dogovorjenim smernicam zdravljenja, da bo le-to lahko kakovostno. Na ta način bomo bolnikom lahko zagotovili tudi hitrejšo dostopnost do zdravnika.

Skoraj v vsakem poglavju poudarjamo, da je za preživetje bolnikov še vedno glavni prognostični dejavnik stadij bolezni. K zgodnejšemu odkrivanju lahko pripomore večja ozaveščenost prebivalstva o zgodnjih znakih bolezni in organizirani presejalni programi.

Presejanje pa je smiselno omogočiti zdravim ljudem le, če je dokazano, da zmanjša umrljivost ali incidenco, če so znana tveganja in koristi in če je strošek v primerjavi s prednostmi sprejemljiv. Trenutno tem merilom zadoščajo: presejanje za raka materničnega vratu s pregledovanjem celic v brisu, ki naj se začne najkasneje po 30. letu starosti in ne pred 20. letom, presejanje za raka dojk z mamografijo za ženske, stare 50 let in več in presejanje za kolorektalni rak z iskanjem prikritih krvavitve v blatu za moške in ženske, stare 50–74 let.

Za zgodnje odkrivanje raka materničnega vratu je bil že leta 1998 pilotno zastavljen program ZORA na širšem območju Ljubljane. Zdaj se širi na celo državo. Uveden je bil poseben Register za izpeljavo in sprotno ocenjevanje tega dela (19). Nedvomno je, da bi z učinkovitim presejalnim programom za raka dojk preživetje lahko še pomembno izboljšali. Upamo, da bo načrt Ministrstva za zdravje na tem področju uspešno izpeljan. Podobno upamo za raka debelega črevesa in danke.

In ne nazadnje, najcenejše zdravljenje je zdravljenje bolezni, ki je ni – primarna preventiva. Za zdravljenje že razvite raka-ve bolezni namreč prihajajo nova, izredno draga zdravila.

Največje breme pri moških predstavljajo kadilski in pivski raki. Ali se bo z novimi zakoni o omejevanju teh razvad stanje izboljšalo? Odstotek moških kadilcev v Sloveniji se je zmanjšal. Vpliv na zbolewnost se že kaže pri pljučnem raku pri moških. Od leta 1995 dalje se je njegova incidenca po 50. letu starosti ustalila. V bodočnosti pa se bojimo, da bo zaradi vse bolj zgodnjega pričetka kajenja mladih vse več tudi mladih bolnikov, starih 30–49 let.

Ali bomo lahko s spremembo prehrabnenih navad in večjo gibalno dejavnostjo med prebivalci Slovenije kaj vplivali na rake prebavnega trakta in dojk?

Zdravstveno-vzgojno delo je izredno pomembno, v ZDA stalno objavljajo tudi študije, v katerih izračunavajo finančni dobrot preventivnih akcij, npr. uspešno izvedenih protika-

CLOSING REMARKS

We, editors of this book, sincerely wish that the data and commentaries will stimulate all specialists that are involved in cancer treatment to get together and start with better, more productive interdisciplinary collaboration. We are most positive that this is the only way to improve the survival of cancer patients in Slovenia.

It is our opinion that in Slovenia cancers that have rather low incidence yet require highly sophisticated treatment, should be treated in one center only (e. g. malignant lymphomas, sarcomas, thyroid cancer, germ cell tumors). The cancers with high incidence (e. g. breast cancer, colorectal cancer, and lung cancer) are treated in several health care centers. However, these centers should have reached the highest proficiency through the treatment of a sufficient number of cancer patients and follow the approved treatment guidelines in order to assure high quality treatment. Such an approach could also assure a faster access of patients to medical treatment.

In almost each chapter, it was specifically stressed that the most important prognostic factor is the disease stage. Early detection of cancer may be noticeably improved by enhancing the awareness of early symptoms of the disease in our population and by launching screening programs.

Screening for cancer in healthy population is reasonable provided that it is definitely sure that it reduces mortality or incidence, and under condition that risks and benefits are well known and that the costs of a screening program versus its benefits are acceptable. Currently, three cancers meet the above requirements: screening for cervical cancer in women aged at least 30 years but not less than 20 by smear test, screening for breast cancer in women aged 50 years and over by mammography, and screening for colorectal cancer in men and women aged between 50 and 74 years by detecting occult fecal bleeding.

In 1998, a pilot study for early detection of cervical cancer named ZORA was outlined for the Ljubljana region and its surroundings. Today, this screening program is being extended all over the country and a special register has been established (19). There is no doubt that we could greatly improve the survival by launching an efficient screening program for breast cancer. We sincerely hope that the project set by the Ministry of Health of the Republic of Slovenia will be successfully implemented. We also expect that similar measures will be adopted also for the colorectal cancer.

Eventually, the least expensive therapy is the treatment of the disease that never develops, in other words, primary prevention. We should be aware that new, extremely expensive drugs are appearing on the market for the treatment of the advanced malignancies.

In men, the heaviest burden are cancers due to heavy smoking and drinking habits. Will there be any turn for the better in restricting these habits with the new law? The percentage of male smokers decreased in Slovenia and its effect has been observed in the lung cancer incidence in men. Since 1995, its incidence has become stable. But we are anxious that the number of young lung cancer patients aged 30–49 years will

dilskih programov med delavci določene tovarne (20). V Sloveniji je preventivnih programov vse več in upajmo, da bodo uspešni.

increase because there are more and more youngsters smoking at a very early age.

Shall we be able to make any step further in the prevention of colorectal and breast cancer by making Slovenian population aware of the urge to change their eating habits and to get more addicted to physical exercise? Health education is of paramount importance. In Slovenia, prevention programs are increasingly propagated and we honestly hope that they will fulfill their mission.

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