

EPIDEMIOLOGIJA RAKA PANKREASA

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SAŽETAK

U svetu, rak pankreasa je sedmi vodeći uzrok umiranja i dvanaesti vodeći uzrok obolevanja među svim malignim tumorima. Stope incidencije i mortaliteta variraju od zemlje do zemlje, što je posledica izloženosti različitim faktorima rizika, mogućnostima ranog dijagnostikovanja i pravovremenog i adekvatnog lečenja. Procenjuje se da će do 2040. godine doći do daljeg porasta broja obolelih (npr. za 27,4% u Evropi) i umrlih (npr. za 28,5% u Evropi) od karcinoma pankreasa. Prema Nacionalnom institutu za karcinome u Sjedinjenim Američkim Državama prosečno petogodišnje preživljavanje za rak pankreasa iznosi 12%. Promenljivi i nepromenljivi faktori doprinose nastanku ovog tumora. Rak pankreasa se češće javlja kod starijih, muškaraca, korisnika duvana i alkohola, osoba sa dijabetesom, preležanim pankreatitisom, fizički neaktivnih i gojaznih, kao i kod osoba sa pozitivnom porodičnom anamnezom za ovaj maligni tumor. Neophodno je raditi na edukaciji stanovništva o faktorima rizika za nastanak raka pankreasa, mogućnostima prevencije i načinu ranog dijagnostikovanja ove bolesti.

Ključne reči: rak pankreasa, incidencija, mortalitet, faktori rizika, preživljavanje, prevencija

Uvod

Rak pankreasa je maligni tumor koji je sedmi vodeći uzrok smrti u svetu od malignih bolesti (1). Prema GLOBOCAN 2020, rak pankreasa je bio na 12. mestu kao najčešći karcinom. (1). U 2020. godini u svetu je dijagnostikovano 495.773 slučajeva raka pankreasa, a kao posledica istog zabeleženo je 466.003 slučajeva smrti (1). Sa starenjem raste broj novoobolelih i umrlih od raka pankreasa, a stope incidencije su veće kod muškaraca nego kod žena (2).

Etiologija karcinoma pankreasa je multifaktorijska i kompleksna. Kao dominantni faktori rizika za nastanak raka pankreasa navode se pušenje i pozitivna porodična anamneza za ovaj maligni tumor (3,4). Rak pankreasa se uglavnom deli na dva tipa: adenokarcinom pankreasa, koji je najčešći (85% slučajeva) koji nastaje u egzokrinim žlezdama pankreasa, i neuroendokrini tumor pankreasa (PanNET), koji je ređi (manje od 5%) i javlja se u endokrinom tkivu pankreasa (5). Karcinom pankreasa ima veoma lošu prognozu, petogo-

dišnje preživljavanje u visoko razvijenoj zemlji kao što je SAD iznosi svega 12,5% (6).

Dijagnoza se postavlja na osnovu imidžing metoda, kao što su kompjuterizovana tomografija, magnetna rezonanca, pozitronska emisiona tomografija i endoskopski ultrazvuk i biopsija iglom (7). Međutim, uglavnom se dijagnoza postavlja tek u uznapredovalom stadijumu (7). U procesu lečenja koriste se hirurške procedure, hemioterapija i biološka terapija, ali su prognoza i preživljavanje kod ovog tumora niski (8).

Cilj ovog preglednog rada je da se sagledaju učestalost i rasprostranjenost ovog malignog tumora, kao i da se identifikuju potencijalni faktori za nastanak ovog oboljenja radi predlaganja odgovarajućih preventivnih mera.

Metode

U okviru ovog preglednog rada za pretraživanje literature korišćena je jedna bibliografska baza podataka PubMed. Pretraživanje literature je spro-

EPIDEMIOLOGY OF PANCREATIC CANCER

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SUMMARY

Pancreatic cancer is the seventh leading cause of cancer-related deaths and the twelfth most common cancer worldwide. Incidence and mortality rates vary from country to country, which is a consequence of exposure to different risk factors, the possibilities of early diagnosis and timely and adequate treatment. It is estimated that by 2040, there will be a further increase in the number of patients (e.g. by 27.4% in Europe) and deaths (e.g. by 28.5% in Europe) caused by pancreatic cancer. According to the National Cancer Institute of the United States of America, the average five-year survival rate for pancreatic cancer is 12%. Modifiable and non-modifiable factors contribute to the occurrence of this tumor. Pancreatic cancer occurs more often in the elderly, men, tobacco and alcohol users, people with diabetes, chronic pancreatitis, physically inactive and obese people, as well as in people with a positive family history of this malignant tumor. It is necessary to work on educating the population about the risk factors for pancreatic cancer, the possibilities of prevention and ways of early diagnosis of this disease.

Key words: pancreatic cancer, incidence, mortality, risk factors, survival, prevention

Introduction

Pancreatic cancer is a malignant tumor that is the seventh leading cause of cancer-related deaths in the world (1). According to GLOBOCAN 2020, pancreatic cancer was the twelfth most common cancer (1). In 2020, 495,773 cases of pancreatic cancer were diagnosed worldwide, and there were 466,003 deaths caused by this tumor (1). The number of new cases and deaths caused by pancreatic cancer increases with age, and the incidence rates are higher in men than in women (2).

The etiology of pancreatic cancer is multifactorial and complex. The dominant risk factors for pancreatic cancer are smoking and a positive family history of this malignant tumor (3,4). Pancreatic cancer is mainly divided into two types: pancreatic adenocarcinoma, which is the most common (85% of cases) and occurs in the exocrine glands of the pancreas, and pancreatic neuroendocrine tumor (PanNET), which is rarer (less than 5%) and occurs in the endocrine tissue of the pancreas (5). Pancreatic cancer has a very

poor prognosis, and the five-year survival rate in the highly developed country such as the USA is only 12.5% (6).

The diagnosis is based on imaging methods, such as computed tomography, magnetic resonance, positron emission tomography and endoscopic ultrasound and needle biopsy (7). However, the diagnosis is usually established only at an advanced stage (7). In the treatment process, surgical procedures, chemotherapy and biological therapy are used, but the prognosis and survival of this tumor are low (8).

The aim of this review article is to assess the incidence and prevalence of this malignant tumor, as well as to identify potential factors for the occurrence of this disease in order to propose appropriate preventive measures.

Methods

Within the scope of this review article, the bibliographic database PubMed was used for the

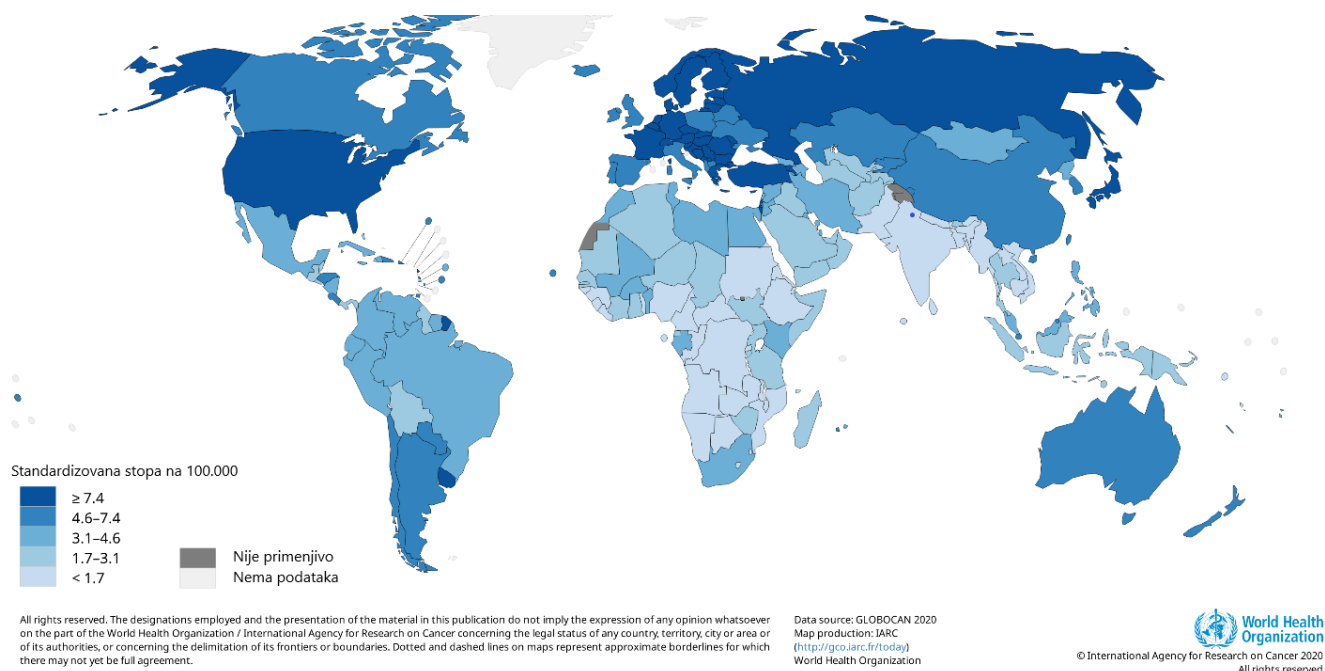
vedeno za poslednjih petnaest godina korišćenjem ključnih reči. U radu su prikazani rezultati samo onih istraživanja koja su bila objavljena na engleskom jeziku.

Incidencija

Incidencija raka pankreasa varira od regiona, pola i godina starosti (1). U 2020. godini, zabeležena su 495.773 nova slučaja karcinoma pankreasa (1). Skoro polovina obolelih (47,1%) bila je iz Azije, 28,3% iz Evrope, 12,6% iz Severne Amerike, dok su oboleli iz Latinske Amerike činili 7,5% obolelih, a iz Afrike 3,4% obolelih (1). Standardizovana stopa incidencije za oba pola u svetu iznosila je 4,9 na 100.000 stanovnika (1). Najniže stope incidencije za rak pankreasa su zabeležene u Južno-Centralnom delu Azije (1,2 na 100.000), i u Srednjoj Africi (1,5 na 100.000), a najveće u Zapadnoj Evropi (8,6 na 100.000) i Severnoj Americi (8,0 na 100.000) (Slika 1). Zemlje sa najvećom stopom incidencije na svetu su Mađarska (11,2 na 100.000), Urugvaj (10,7 na 100.000), i Japan (9,9 na 100.000), a sa najnižom su Bocvana (0,66 na 100.000), Vanuatu (0,64 na 100.000), i Malavi (0,63 na 100.000). Globalno, stope incidencije su veće kod muškaraca (5,7 na 100.000) nego kod žena (4,1 na 100.000) (1). Ova bolest se skoro ne dijagnostikuje pre 55. godine života, a potom incidencija raste i najveća je posle 70. godine (2).

U Republici Srbiji, rak pankreasa je na 7. mestu na osnovu broja obolelih od svih malignih bolesti i čini 3,5% svih novotkrivenih slučajeva karcinoma, sa incidencijom od 8,5 na 100.000 (1,9). U Republici Srbiji je u 2020. godini broj novoobolelih od raka pankreasa iznosio 1.453, i to 791 kod muškaraca, i 662 kod žena. Standardizovana stopa incidencije je bila veća kod muškaraca i iznosila je 11,3 na 100.000, dok je kod žena bila 7,9 na 100.000 (9). Najviše uzrasno-specifične stope incidencije bile su kod starijih od 70 godina (9).

Još uvek nije jasno zašto toliko varira stopa incidencije raka pankreasa u različitim regionima i po polu. Pretpostavlja se da je to zato što je u svetu različita izloženost faktorima rizika. Žene su manje izložene faktorima rizika iz okruženja odgovornim za njihov nastanak ili manje sklone ovakvim malignim tumorima, kao na primer korišćenje cigareta. Cigarete češće konzumiraju muškarci i češće obolevaju od karcinoma pankreasa (10). Još jedna stvar koju treba uzeti u obzir je da dostupnost dijagnostičkih metoda varira između razvijenih i nerazvijenih geografskih područja. Štaviše, neke razlike u procenjenoj incidenciji mogu se pripisati kvalitetu registara, jer se obuhvat, potpunost i tačnost razlikuju od zemlje do zemlje (11).



Slika 1. Procenjena standardizovana stopa incidencije (prema populaciji sveta) za 2020. godinu za rak pankreasa za oba pola i sve uzraste (Izvor: GLOBOCAN 2020; <https://gco.iarc.fr/today>)

search of literature. The literature search was conducted for the last fifteen years using the key words. Only the results of studies that were published in the English language were included in this article.

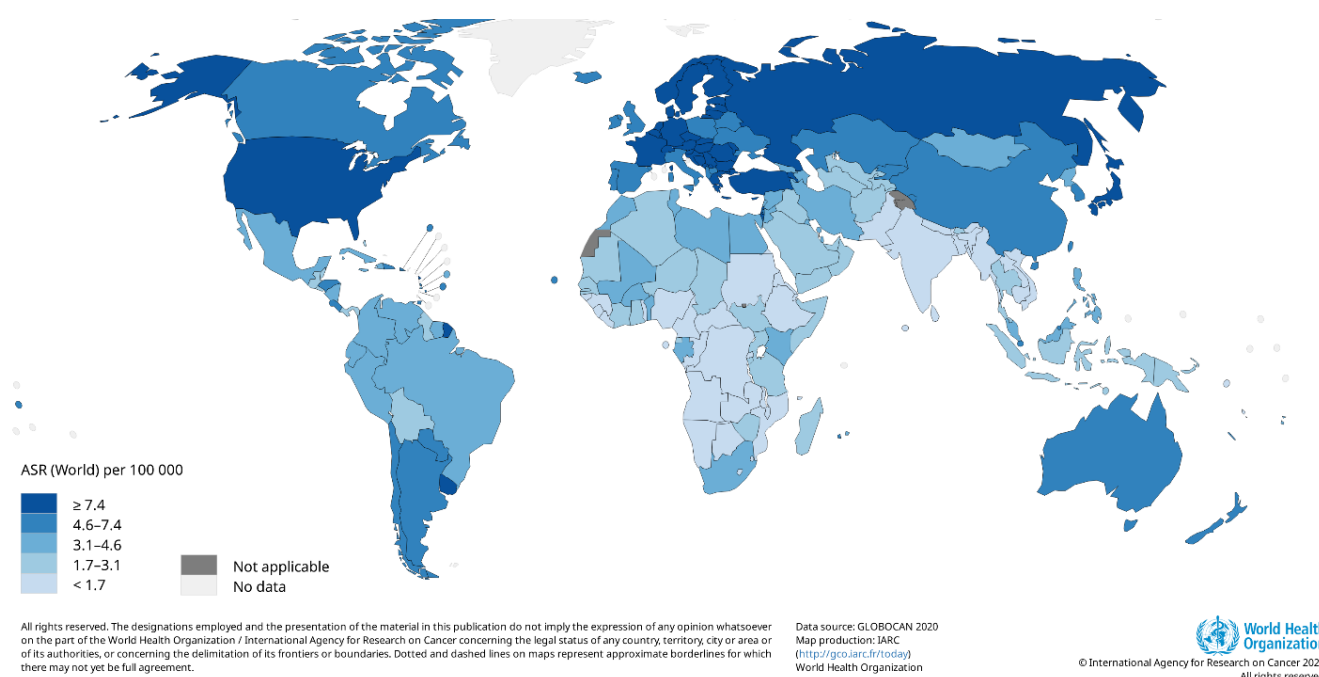
Incidence

The incidence of pancreatic cancer varies by region, gender and age (1). In 2020, 495,773 new cases of pancreatic cancer were recorded (1). Almost half of the patients (47.1%) were from Asia, 28.3% were from Europe, 12.6% from North America, while 7.5% of patients were from Latin America, and 3.4% of patients from Africa (1). In the world, the standardized incidence rate for both sexes was 4.9 per 100,000 inhabitants (1). The lowest incidence rates for pancreatic cancer were registered in the South-Central part of Asia (1.2 per 100,000), and in Central Africa (1.5 per 100,000), while the highest rates were in Western Europe (8.6 per 100,000) and North America (8.0 per 100,000) (Picture 1). The countries with the highest incidence rate in the world are Hungary (11.2 per 100,000), Uruguay (10.7 per 100,000), and Japan (9.9 per 100,000), while the lowest rates are in Botswana (0.66 per 100,000), Vanuatu (0.64 per 100,000), and Malawi (0.63 per 100,000). Globally, the incidence rates are higher in men (5.7

per 100,000) than in women (4.1 per 100,000) (1). This disease is almost never diagnosed before the age of 55, and then the incidence increases and is the highest after the age of 70 (2).

In the Republic of Serbia, pancreatic cancer is the 7th most common malignant tumor and it accounts for 3.5% of all newly diagnosed cancer cases, with the incidence of 8.5 per 100,000 (1,9). In 2020, in the Republic of Serbia, the number of new cases of pancreatic cancer amounted to 1,453, that is, 791 of men and 662 of women. The standardized incidence rate was higher in men and it was 11.3 per 100,000, while in women it was 7.9 per 100,000 (9). The highest age-specific incidence rates were in people older than 70 (9).

It is still not clear why the incidence rate of pancreatic cancer varies so much by gender and in different regions. It is assumed that it is the case because exposure to risk factors is different across the world. Women are less exposed to environmental risk factors responsible for its occurrence, such as smoking, or less prone to these malignant tumors. Cigarettes are more often used by men and they are more likely to get pancreatic cancer (10). Another thing that should be considered is that the availability of diagnostic tools varies between developed and underdeveloped geographic regions. Furthermore,



Picture 1. Estimated standardized incidence rate (according to the world population) for the year 2020 for pancreatic cancer, both sexes, all ages (Source: GLOBOCAN 2020; <https://gco.iarc.fr/today>)

Mortalitet

Mortalitet raka pankreasa varira od regiona, pola i godina starosti (1). U 2020. godini, zabeleženo je 466.003 smrti od karcinoma pankreasa, sa standardizovanom stopom mortaliteta od 4,5 na 100.000 stanovnika (1). U Južno-Centralnoj Aziji zabeležena je najmanja stopa mortaliteta za rak pankreasa (1,1 na 100.000), i u Srednjoj Africi (1,5 na 100.000), a najveća u Zapadnoj Evropi (7,8 na 100.000) i Severnoj Americi (6,5 na 100.000). Mađarska i Urugvaj su zemlje sa najvećom stopom mortaliteta u svetu (10,2 na 100.000), a Malavi sa najmanjom (0,62 na 100.000) (Slika 2). Stope mortaliteta su veće kod muškaraca (5,3 na 100.000) u odnosu na žene (3,8 na 100.000) (1).

U Republici Srbiji, rak pankreasa je na 4. mestu prema broju umrlih od malignih bolesti i čini 5,6% svih umrlih usled malignih bolesti, sa standardizovanom stopom mortaliteta od 8 na 100.000 (1,9). U 2020. godini, u Republici Srbiji je broj umrlih od raka pankreasa iznosio 1169 (625 muškaraca i 544 žena). Standardizovana stopa mortaliteta za rak pankreasa je bila veća kod muškaraca i iznosila je 8,5 na 100.000, dok je kod žena bila 5,4 na 100.000 (9). U periodu 1999-2019. godine, u Centralnoj Srbiji stopa mortaliteta je bila najveća kod starijih od 70 godina i to kod oba pola (12).

Primećuje se da su stope incidencije i mortaliteta slične. To ide u prilog činjenici da se ova

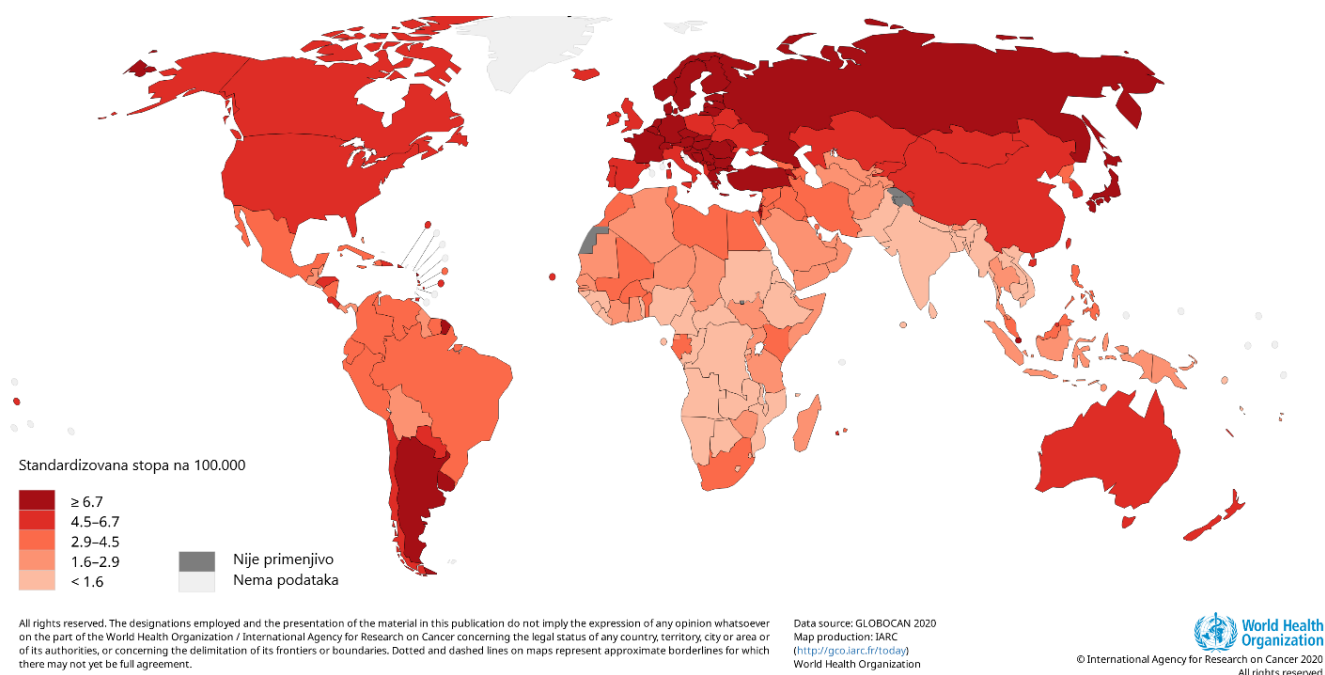
bolest teško leči, otkriva se u kasnijim stadijumima zbog nespecifičnih simptoma, pacijenti su većinom stariji i sa narušenim zdravljem (13).

Kretanje obolevanja i umiranja od raka pankreasa

U poslednje dve decenije primećen je rast stopa incidencije i mortaliteta raka pankreasa i on je različit po regionima sveta. U SAD, standardizovane stope incidencije su bile u blagom porastu od 0,9% godišnje u periodu 2010-2019, dok su stope mortaliteta rasle prosečno 0,1% godišnje u periodu 2011-2020. godine (6).

Predviđanje opterećenja karcinomom pankreasa u sveta govori da će broj obolelih i umrlih biti znatno veći u 2040. godini (Slike 3 i 4). Najveći rast broja obolelih u 2040. godini, u odnosu na 2020. godinu, očekuje se u Africi (+100,1%), zatim u Latinskoj Americi i karibima (+81,6%) i u Aziji (+81,5%), a najmanji u Evropi (+27,4%). Najveći rast broja umrlih u 2040. godini, u odnosu na 2020. godinu, očekuje se u Africi (+100,7%), a najmanji u Evropi (+28,5%) (14).

U Centralnoj Srbiji, u periodu od 1999-2019. godine, stope incidencije i mortaliteta za rak pankreasa su bile u porastu. Kod muškaraca stopa incidencije za rak pankreasa je prosečno rasla za 2,9% godišnje, a kod žena za 3,7%. Stope mortaliteta za rak pankreasa su prosečno rasle za +1,2% godišnje



Slika 2. Procenjena standardizovana stopa mortaliteta (prema populaciji sveta) za 2020. godinu za rak pankreasa za oba pola i sve uzraste (Izvor: GLOBOCAN 2020; <https://gco.iarc.fr/today>)

some differences in the estimated incidence may be attributed to the quality of registries, because coverage, completeness and accuracy vary between different countries (11).

Mortality

The mortality of pancreatic cancer varies by region, sex and age (1). In 2020, 466,003 deaths caused by pancreatic cancer were registered, with the standardized mortality rate of 4.5 per 100,000 (1). The lowest mortality rate of pancreatic cancer was registered in South-Central Asia (1.1 per 100,000), and in Central Africa (1.5 per 100,000), while the highest was in Western Europe (7.8 per 100,000) and North America (6.5 per 100,000). Hungary and Uruguay are the countries with the highest mortality rate in the world (10.2 per 100,000), while the lowest rate is in Malawi (0.62 per 100,000) (Picture 2). Mortality rates are higher in men (5.3 per 100,000) in comparison to women (3.8 per 100,000) (1).

In the Republic of Serbia, pancreatic cancer ranks 4th in terms of the number of deaths caused by malignant diseases, and it accounts for 5.6% of all cancer-related deaths, with the standardized mortality rate of 8 per 100,000 (1,9). In 2020, in the Republic of Serbia, the number of deaths caused by pancreatic cancer was 1169 (625 men and 544 women). The standardized mortality rate

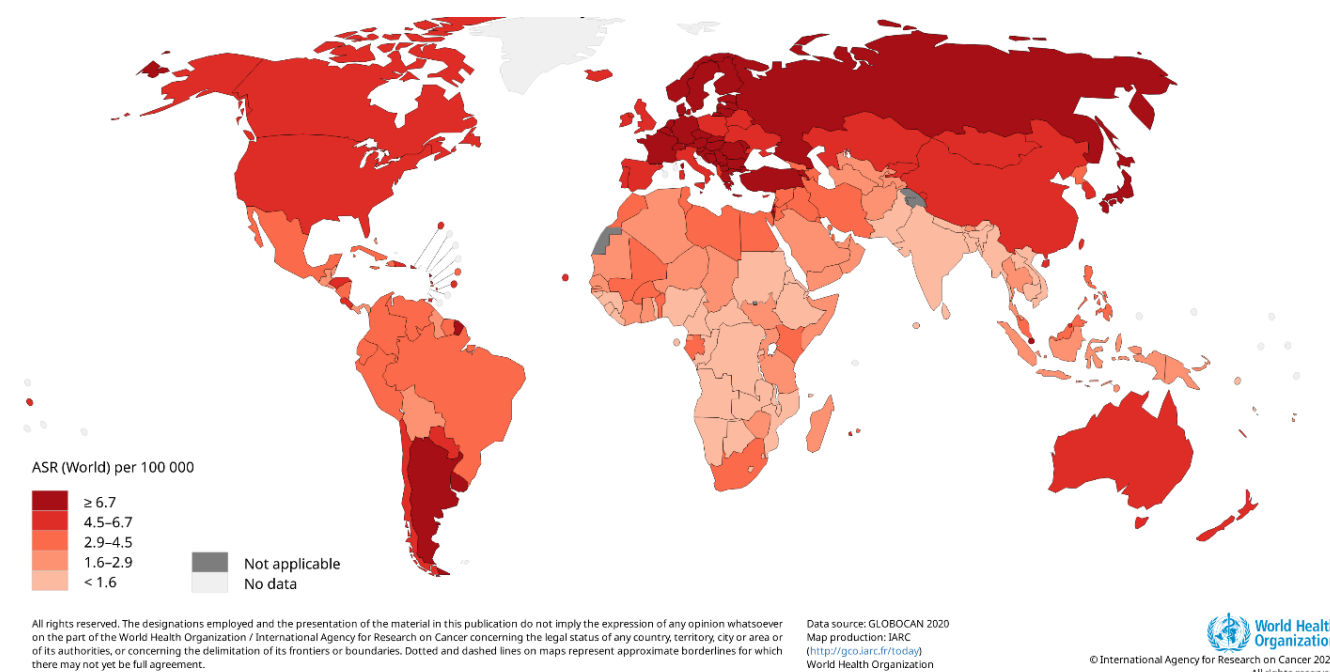
of pancreatic cancer was higher in men and it amounted to 8.5 per 100,000, while in women it was 5.4 per 100,000 (9). In the period 1999-2019, in Central Serbia, the mortality rate was the highest in persons older than 70 years in both sexes (12).

It has been noticed that incidence and mortality rates are similar. This is in favor of the fact that this disease is hard to cure, it is discovered in later stages due to non-specific symptoms, and patients are mostly the elderly with the impaired health (13).

Trends in pancreatic cancer incidence and mortality

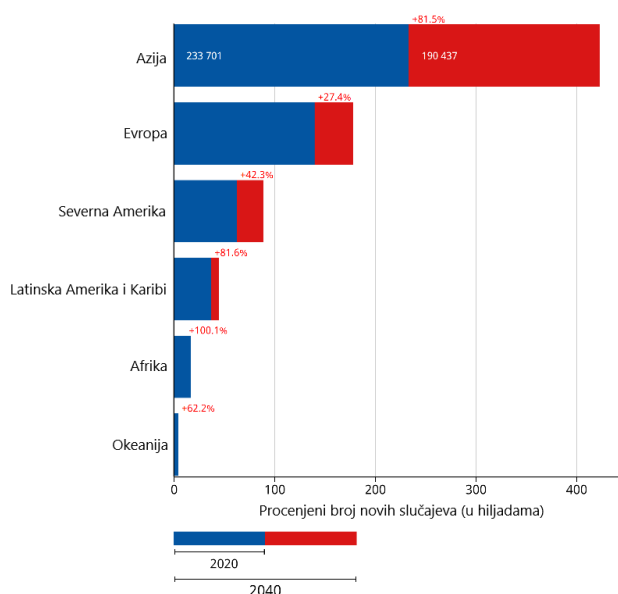
An increase in incidence and mortality rates of pancreatic cancer has been noticed in the last two decades, and it varies by regions of the world. In the USA, standardized incidence rates increased slightly, that is, 0.9% per year in the period 2010-2019, while mortality rates increased, on average, by 0.1% per year in the period 2011-2020 (6).

Estimates of the burden of pancreatic cancer in the world predict that the number of new cases and deaths will be significantly higher in 2040 (Pictures 3 and 4). The highest increase in the number of new cases in 2040 in comparison to 2020 is expected in Africa (+100.1%), followed by Latin America and the Caribbean (+81.6%) and Asia (+81.5%), while the lowest is expected in Europe (+27.4%). The largest increase in the number of



Picture 2. Estimated standardized mortality rate (by the world population) in 2020 for pancreatic cancer, for both sexes, all ages (Source: GLOBOCAN 2020; <https://gco.iarc.fr/today>)

Procenjeni broj novih slučajeva od 2020. do 2024. godine, oba pola, uzrast 0-85+ godina
Pankreas

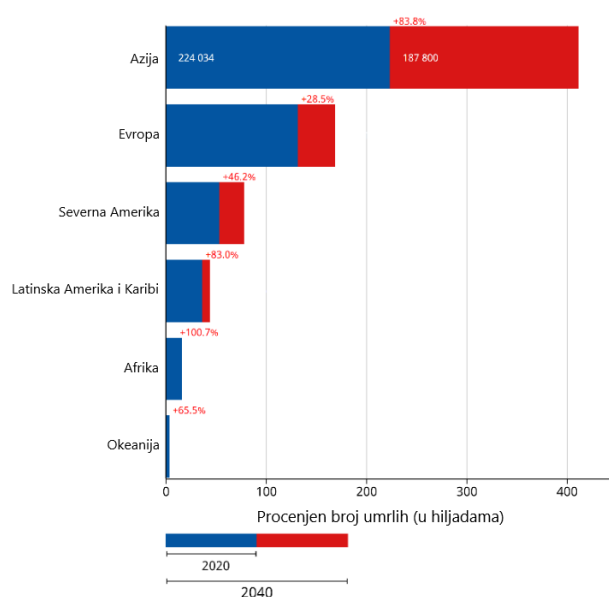


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International Agency for Research on Cancer
World Health Organization

Slika 3. Trend porasta broja obolelih od raka pankreasa po regionima sveta od 2020. do 2040. godine
(Izvor: IARC - Cancer tomorrow; <https://gco.iarc.fr/tomorrow>)

Procenjeni broj umrlih od 2020. do 2040. godine, oba pola, uzrast 0-85+ godina
Pankreas



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World Health Organization

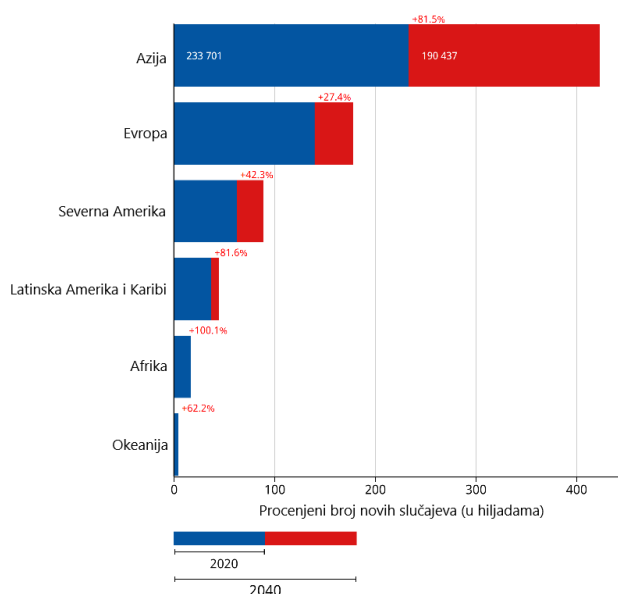
Slika 4. Trend porasta broja umrlih od raka pankreasa po regionima sveta od 2020. do 2040. godine
(Izvor: IARC - Cancer tomorrow; <https://gco.iarc.fr/tomorrow>)

kod muškaraca, a za +0,6% kod žena, ali je samo kod muškaraca utvrđen značajan porast (12). Procenjuje se da će se u Republici Srbiji broj obolelih povećati za 8,9%, a broj umrlih za 9,5% do 2040. godine, u odnosu na 2020. godinu (14).

Različit trend rasta broja obolelih i umrlih od raka pankreasa objašnjava se različitom distribucijom faktora rizika. Konzumiranje cigareta je pre-

poznato kao najznačajniji faktor rizika za nastanak ovog karcinoma i smatra se da se smanjenjem prevalencije korisnika cigareta može prevenirati i karcinom pankreasa. Pored pušenja cigareta, alkohol, ishrana bogata zasićenim masnim kiselinama i nedovoljno sprovođenje fizičke aktivnosti utiču na oboljevanje. Zanimljivo je da se procenjuje najveći porast oboljevanja i umiranja u Africi, koja je u fazi

Procenjeni broj novih slučajeva od 2020. do 2024. godine, oba pola, uzrast 0-85+ godina
Pankreas

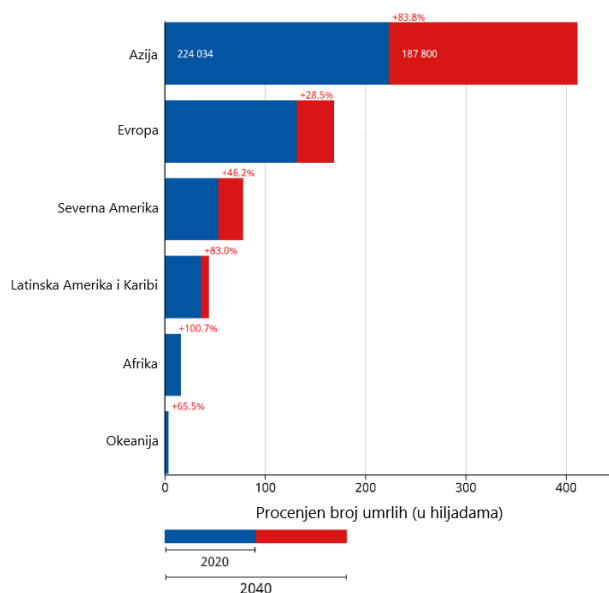


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Picture 3. Rising trends in pancreatic cancer incidence by world regions from 2020 to 2040
(Source: IARC - Cancer tomorrow; <https://gco.iarc.fr/tomorrow>)

Procenjeni broj umrlih od 2020. do 2040. godine, oba pola, uzrast 0-85+ godina
Pankreas



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World Health Organization

Picture 4. Rising trends in pancreatic cancer mortality by world regions from 2020 to 2040
(Source: IARC - Cancer tomorrow; <https://gco.iarc.fr/tomorrow>)

deaths in 2040, in comparison to 2020, is expected in Africa (+100.7%), while the lowest is expected in Europe (+28.5%) (14).

In the period 1999-2019, in Central Serbia, incidence and mortality rates of pancreatic cancer increased. In men, the incidence rate of pancreatic cancer increased, on average, by 2.9% per year, and in women by 3.7%. Mortality rates

of pancreatic cancer increased, on average, by +1.2% per year in men, and by +0.6% in women, but a significant increase was found only in men (12). It is estimated that in the Republic of Serbia, the number of new cases will increase by +8.9%, while the number of deaths will increase by 9.5% by 2040, in comparison to 2020 (14).

The different trend of increase in the number

razvoja i tako ima ograničene pristupe dijagnostici i lečenju. Mogući načini da se ovaj trend obolevanja smanji jeste da se prevenira promenom načina života i poboljša svest o bolesti i njenim simptomima, kako bi se dijagnostikovala u ranijim stadijumima (2).

Preživljavanje

Karcinom pankreasa je oboljenje visoke smrtnosti. Petogodišnje preživljavanje u periodu od 2014-2018. godine je poboljšano sa 6% na 9%, što pokazuje da je napredak moguć i da je postignut (2).

Preživljavanje zavisi od puno faktora, a jedan od najznačajnijih je stadijum u kojem se bolest otkriva. Prema Nacionalnom institutu za karcinome u SAD-u prosečno petogodišnje preživljavanje je 12,5%. Ako je karcinom dijagnostikovao u ranoj fazi, kada je hirurško odstranjivanje moguće, petogodišnje preživljavanje je 44,3%. Ako se karcinom proširio na okolna tkiva i organe, petogodišnje preživljavanje je 16,2%. Međutim, 51% obolelih u trenutku dijagnostikovanja ima udaljene metastaze, i kod njih petogodišnje preživljavanje iznosi oko 3,2% (6).

Etiologija i faktori rizika

Faktori rizika za nastanak raka pankreasa se mogu podeliti na promenljive i nepromenljive, u odnosu na to da li možemo ili ne da ih preveniramo (2). Pušenje predstavlja najrasprostranjeniji i najvažniji faktor rizika za nastanak karcinoma pankreasa. U meta analizi iz 2012. godine, pokazano je da je rizik od nastanka karcinoma pankreasa 2,2 puta veći kod trenutnih pušača i 1,17 puta kod bivših pušača u odnosu na nepušače (3). Rizik za nastanak karcinoma pankreasa se povećava sa većim brojem popušanih cigareta dnevno i sa dužim pušačkim stažom (3). Nema povezanosti sa godinama života kada je osoba počela sa konzumiranjem cigareta (3).

Konzumiranje alkohola je povezano sa nastankom karcinoma pankreasa. Osobe koje piju više od 4 jedinice alkohola dnevno (jedna jedinica alkohola je 14,8 ml čistog etanola u navedenom piću) su u većem riziku od onih koji piju manje. Rizik je znatno povećan kod osoba koje konzumiraju 9 i više jedinica alkohola dnevno. Što se tiče vrste alkoholnog pića, osobe koje konzumiraju više od 4 jedinice vina su u većem riziku od nastanka karcinoma pankreasa, dok porast rizika nije primećen za konzumaciju piva ili žestokog pića (15).

Povećana telesna težina i veći indeks telesne mase (ITM) povezani su sa većim rizikom od nastanka karcinoma pankreasa za razliku od osoba koje imaju normalne vrednosti ITM. Čak su i veći obim struka i veći odnos obima struka i kukova povezani sa nastankom ovog karcinoma (16).

Povećano konzumiranje crvenog mesa (više od 120 gr dnevno) i prerađenog mesa (više od 50 gr dnevno) su povezani sa nastankom karcinoma pankreasa (17). U Ujedinjenom Kraljevstvu je na osnovu podataka dve velike prospektivne studije (ukupno 60.310 ispitanika) zaključeno da je manji mortalitet od ove bolesti kod osoba koje jedu manje mesa ili su vegeterijanci ili vegani (18).

Ostali promenljivi faktori sa kojima je povezano oboljevanje od raka pankreasa jesu fizička neaktivnost i profesionalna izloženost nekim supstancama (npr. nikl, kadmijum, arsen, hlorisani organski rastvarači, formaldehid) (2,19).

U nepromenljive faktore rizika za nastanak raka pankreasa spadaju pol, uzrast, komorbiditeti, pozitivna porodična anamneza za ovaj maligni tumor, itd. Muškarci češće obolevaju od karcinoma pankreasa nego žene (1,2,20). Smatra se da su muškarci češće izloženi faktorima rizika (pušenju i alkoholu) u odnosu na žene i da je zato kod njih veća stopa incidencije nego kod žena (2). Ova bolest se gotovo i ne javlja kod osoba mlađih od 55. godina, što znači da se sa starenjem povećava mogućnost nastanka ove bolesti (1,2,20,21). Mnoge studije potvrđuju povezanost šećerne bolesti i nastanka karcinoma pankreasa. Ovaj rizik je znatno povećan kod osoba koje duže vreme boluju od dijabetesa melitusa (19). Osobe sa pozitivnom porodičnom istorijom u vezi javljanja karcinoma pankreasa su u većem riziku za nastanak raka pankreasa za razliku od osoba koje nemaju ovu bolest u porodici. Bolest se češće javlja kod srodnika prve linije u odnosu na dalje krvne srodnike (4). Ostali nepromenljivi faktori za nastanak raka pankreasa su pankreatitis, infekcija *H. pylori*, infekcija uzrokovana hepatitis B i C virusom, prisustvo određenih mutacija i dr. (2,19).

Prevenција

Rana dijagnoza karcinoma pankreasa bi mogla smanjiti mortalitet, poboljšati preživljavanje i kvalitet života osoba sa karcinomom pankreasa. Međutim, skrining opšte populacije ne bi doneo očekivane rezultate i zato bi trebalo izabrati rizičnu grupu koju treba podvrgnuti testiranju, kao što su bliski srodnici obolelih i oni koji su izloženi faktori-

of new cases and deaths caused by pancreatic cancer is explained by different distribution of risk factors. Smoking has been recognized as the most significant risk factor for the occurrence of this cancer, and it is believed that pancreatic cancer can be prevented by reducing the prevalence of tobacco users. In addition to smoking, alcohol, a diet rich in saturated fatty acids and insufficient physical activity influence the occurrence of this disease. It is interesting that the highest increase in morbidity and mortality is estimated in Africa, which is a developing country, and thus has limited access to diagnostics and treatment. Possible ways to reduce this disease trend is to prevent it by changing the lifestyle and by improving the awareness regarding this disease and its symptoms, in order to diagnose it in earlier stages (2).

Survival

Pancreatic cancer is a disease with high mortality. Five-year survival in the period 2014-2018 improved from 6% to 9%, which shows that improvement is possible and has been achieved (2).

Survival depends on many factors and one of the most important is the stage at which the disease is detected. According to the National Cancer Institute in the USA, the average five-year survival rate is 12.5%. If cancer is diagnosed at an early stage, when surgical removal is possible, the five-year survival rate is 44.3%. If the cancer has spread to surrounding organs and tissues, the five-year survival rate is 16.2%. However, 51% of patients have distant metastases at the moment of diagnosis, and their five-year survival is about 3.2% (6).

Etiology and risk factors

Risk factors for pancreatic cancer may be divided into modifiable and non-modifiable, in relation to whether we can prevent them or not (2). Smoking is the most common and important risk factor for the occurrence of pancreatic cancer. In one meta-analysis from 2012, it was shown that the risk of developing pancreatic cancer is 2.2 times higher in current smokers and 1.17 times higher in former smokers in comparison to non-smokers (3). The risk of developing pancreatic cancer increases with a greater number of cigarettes smoked per day and with a longer history of smoking (3). It is not associated with the age when a person started smoking cigarettes (3).

Alcohol consumption is associated with the occurrence of pancreatic cancer. Persons who drink more than 4 units of alcohol per day (one unit of alcohol is 14.8 ml of pure ethanol in that drink) are at an increased risk compared to those who drink less. The risk is significantly higher in persons who consume 9 units of alcohol or more per day. As far as the type of alcoholic beverage is concerned, persons who consume more than 4 units of wine are at an increased risk of developing pancreatic cancer, while the increase of this risk was not noted for beer or other spirits (15).

The increased body weight and higher body mass index (BMI) are associated with a higher risk of pancreatic cancer, as opposed to people who have normal BMI values. Even a bigger waist circumference and a higher waist-to-hip ratio are associated with the occurrence of this cancer (16).

The increased consumption of red meat (more than 120 g per day) and processed meat (more than 50 g per day) are associated with the development of pancreatic cancer (17). In the United Kingdom, based on the data from two large prospective studies (60,310 participants), it was concluded that the mortality of this disease is lower in persons who eat less meat or who are vegetarians or vegans (18).

Other modifiable factors associated with pancreatic cancer are physical inactivity and occupational exposure to certain substances (e.g. nickel, cadmium, chlorinated organic solvents, formaldehyde) (2,9).

Non-modifiable risk factors for the occurrence of pancreatic cancer include sex, age, comorbidities, positive family history of this malignant tumor etc. Men are more likely to suffer from pancreatic cancer than women (1,2,20). It is believed that men are more exposed to risk factors (smoking and alcohol) than women, and due to this fact they have a higher incidence rate than women (2). This disease almost does not occur in persons younger than 55, which means that the possibility of the occurrence of this disease increases with age (1,2,20,21). Many studies confirm the connection between diabetes and pancreatic cancer. This risk is significantly increased in people who have suffered from diabetes mellitus for a longer period of time (19). Persons with a positive family history of pancreatic cancer are at an increased risk of developing this disease in contrast to persons who do not have this disease in their family. The

ma rizika (2,22). Bilo bi idealno formirati starostnu granicu kada se treba podvrgnuti testiranju i koliko često kod familijarnog karcinoma, kao i koliko dugo nakon dijagnoze dijabetes melitusa (22).

Međutim, i primarna prevencija ima velikog udela u sprečavanju nastanka bolesti. Najvažniji faktor rizika je pušenje cigareta (3). Prestankom pušenja cigareta se smanjuje i rizik nastanka ove bolesti. Ostali promenljivi faktori se takođe mogu korigovati i smanjiti mogućnost nastanka ove bolesti. Međutim, kod osoba koje imaju genetsku predispoziciju za nastanak ove bolesti, osim menjanja stila života i životnih navika, oni ne mogu značajno uticati na nastanak ove bolesti i za njih bi skrining bio idealan postupak za rano otkrivanje i lečenje (23).

Zaključak

Karcinom pankreasa je čest maligni tumor i preživljavanje je vrlo nisko. Na osnovu epidemioloških podataka, očekuje se znatan porast obolelih u narednom periodu, ali se smatra da će se poboljšati mogućnosti lečenja i smanjiti smrtnost od ovog karcinoma. Neophodno je raditi na edukaciji stanovništva o faktorima rizika za nastanak raka pankreasa, mogućnostima prevencije i načinu ranog dijagnostikovanja ove bolesti.

Konflikt interesa

Autori su izjavili da nema konflikta interesa.

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disease occurs more often in the first-line relatives in comparison to more distant relatives (4). Other non-modifiable risk factors for the development of pancreatic cancer are pancreatitis, H. pylori infection, infection caused by hepatitis B and C virus, the presence of certain mutations, etc. (2,19).

Prevention

Early diagnosis of pancreatic cancer could reduce mortality, improve the survival and quality of life of persons with pancreatic cancer. However, screening the general population would not yield the expected results, and therefore, a risk group should be selected for testing, such as close relatives of the affected and those exposed to risk factors (2,22). It would be ideal to establish the age limit when to do testing and how often in case of hereditary cancer, as well as how long after the diagnosis of diabetes mellitus (22).

However, primary prevention also plays a major role in preventing the onset of disease. The most important risk factor is smoking (3). Stopping smoking reduces the risk of developing this disease. Other modifiable risk factors can also be corrected, thus reducing the possibility of the occurrence of this disease. However, in persons who have a genetic predisposition of this disease, apart from changing their lifestyle and habits, they cannot significantly influence the onset of this disease and for them screening would be an ideal procedure for early detection and treatment (23).

Conclusion

Pancreatic cancer is a common malignant tumor and survival is very low. Based on the epidemiological data, a significant increase in the number of new cases is expected in the following period, however, it is believed that treatment options will be improved and that mortality will decrease. It is necessary to work on educating the population about risk factors for pancreatic cancer, the possibilities of prevention and ways of early diagnosis of this disease.

Competing interests

The authors declared no competing interests.

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