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KRETANJE OBOLEVANJA I UMIRANJA OD KOLOREKTALNOG KARCINOMA KOD MUŠKARACA I ŽENA CENTRALNE SRBIJE ZA PERIOD 1999-2020. GODINE

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SAŽETAK

Uvod/Cilj: Kolorektalni karcinom je treći vodeći maligni tumor po obolevanju u svetu, odmah posle karcinoma dojke i pluća, i drugi vodeći maligni tumor prema broju umrlih, iza raka pluća. Cilj ove deskriptivne studije je bio da se analizira kretanje obolevanja i umiranja od karcinoma kolorektuma kod muškaraca i žena Centralne Srbije u periodu od 1999. do 2020. godine.
Metode: Podaci o obolelima i umrlima od kolorektalnog karcinoma (šifre C18 - C20, prema Internacionalnoj klasifikaciji bolesti), kao i o broju stanovnika, po polu i uzrastu, za period od 1999. do 2020. godine, preuzeti su iz registara za rak u Centralnoj Srbiji i od Instituta za javno zdravlje Srbije „Dr Milan Jovanović Batut". Izračunate su sirove, uzrasno-specifične i standardizovane stope incidencije i mortaliteta za rak kolorektuma. U cilju analize kretanja stopa incidencije i mortaliteta korišćena je *joinpoint* regresiona analiza.
Rezultati: U periodu od 1999. do 2020. godine u Centralnoj Srbiji je od kolorektalnog karcinoma prosečno obolevalo 1696 muškaraca i 1112 žena, a umiralo 990 muškaraca i 676 žena. Prosečna standardizovana stopa incidencije (na 100.000) je bila 34,4 za muškarce i 19,5 za žene, a prosečna standardizovana stopa mortaliteta (na 100.000) 18,4 za muškarce i 10,1 za žene. Prosečne uzrasno specifične stope incidencije i mortaliteta od kolorektalnog karcinoma rastu sa godinama starosti kod oba pola. U periodu 1999-2020. godine, standardizovane stope incidencije kolorektalnog karcinoma značajno rastu za 0,7% godišnje za žene i 1% godišnje za muškarce. Kod žena uočava se značajan porast stopa mortaliteta od kolorektalnog karcinoma od 2,6% godišnje u periodu 1999-2006. godine, a potom pad od 1,2% godišnje za period 2006-2020. Međutim, kod muškaraca se uočava značajan porast u periodu 1999-2010., a zatim pad od 1,2% godišnje, ali bez statističke značajnosti.
Zaključak: Neophodno je raditi na unapređenju sprovođenja organizovanog skrininga za rak kolorektuma, kao i na edukaciji stanovništva o faktorima rizika za nastanak ovog malignoma i mogućnostima prevencije.

Ključne reči: kolorektalni karcinom, incidencija, mortalitet, trend, joinpoint regresiona analiza

Uvod

Prema podacima GLOBOCAN-a za 2020. godinu, od malignih tumora u svetu je obolelo blizu 20 miliona ljudi (1). Iste godine od kolorektalnog karcinoma obolelo je skoro 2 miliona ljudi (1.931.590 novoobolelih), što čini 10% svih novoobolelih od malignih tumora. U 2020. godini, broj novoobolelih od kolorektalnog karcinoma u populaciji muškaraca u svetu je bio 1.065.960, dok je obolelih žena bilo 865.630. Kolorektalni karcnom je treći vodeći uzrok obolevanja od malignih tumora u svetu, odmah posle karcinoma dojke i pluća, kada se oba pola posmatraju zajedno (1). Treći je vodeći uzrok obolevanja u muškoj populaciji, iza karcinoma pluća i prostate, a drugi u populaciji žena, iza karcinoma dojke (1). U svetu je, 2020. godine, od karcinoma debelog creva umrlo 973.173 osoba, što čini 9,4% svih umrlih od malignih tumora (1). Umrlih muškaraca bilo je 515.637, a žena 419.536 (1). I pored postojanja savremenih metoda skrininga koje bi u velikoj meri mogle smanjiti umira-

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TRENDS IN MORBIDITY AND MORTALITY OF COLORECTAL CANCER IN MEN AND WOMEN OF CENTRAL SERBIA DURING THE PERIOD 1999-2020

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SUMMARY

Introduction/Aim: Colorectal cancer is the third leading cancer in terms of morbidity in the world, right after breast and lung cancer, and the second leading malignant tumor according to the number of deaths, after lung cancer. This descriptive study aimed to analyze the trends in incidence and mortality from colorectal cancer in men and women in Central Serbia from 1999 to 2020.
Methods: Data on patients and deaths from colorectal cancer (codes C18-C20, according to the International Classification of Diseases), as well as on the number of inhabitants, by sex and age, for the period from 1999 to 2020, were taken from cancer registries in Central Serbia and at the request of the Institute for Public Health of Serbia "Dr. Milan Jovanović Batut". Crude, age-specific and standardized incidence and mortality rates for colorectal cancer were calculated. In order to analyze trends in incidence and mortality rates, joinpoint regression analysis was used.
Results: In the period from 1999 to 2020 in Central Serbia, an average of 1696 men and 1112 women were diagnosed with colorectal cancer, and 990 men and 676 women died. In the mentioned period, the average standardized incidence rate (per 100,000) was 34.4 for men and 19.5 for women, and the average standardized mortality rate (per 100,000) was 18.4 for men and 10.1 for women. Average age-specific incidence and mortality rates from colorectal cancer increase with age in both sexes. In the period 1999-2020, the standardized incidence rates of colorectal cancer are increasing significantly by 0.7% per year for women and 1% per year for men. In women, a significant increase in the mortality rate from colorectal cancer of 2.6% per year is observed in the period 1999-2006 year, and then a decline of 1.2% per year for the period 2006-2020. However, in men, a significant increase is observed in the period 1999-2010, followed by a decrease of 1.2% per year, but without statistical significance.
Conclusion: It is necessary to work on improving the implementation of organized screening for colorectal cancer, as well as on educating the population about the risk factors for the occurrence of this malignancy and the possibilities for prevention.

Keywords: colorectal cancer, incidence, mortality, trend, joinpoint regression analysis

Introduction

According to GLOBOCAN data for 2020, nearly 20 million people fell ill with malignant tumors worldwide (1). In the same year, almost 2 million people (1,931,590 new cases) were diagnosed with colorectal cancer, which is 10% of all new cases of malignant tumors. In 2020, the number of new cases of colorectal cancer in the population of men was 1,065,960 in the world, while the number of women was 865,630. Colorectal cancer is the third leading cause of morbidity of malignant tumors in the world, right after breast and lung cancer, when both sexes are considered together (1). It is the third leading cause of morbidity in men, after lung and prostate cancer, and the second in the female population, after breast cancer (1). In 2020, 973,173 people died from colorectal cancer worldwide, which is 9.4% of all deaths from malignant tumors (1). There were 515,637 men who died, and 419,536 women (1). Despite the existence of modern screening methods that

nje od ovog tumora, danas kolorektalni karcinom predstavlja drugi vodeći uzrok umiranja među svim malignim tumorima u svetu, iza karcinoma pluća, kada se posmatraju oba pola (1). Međutim, kod muškaraca je treći vodeći uzrok umiranja, iza raka pluća i jetre, a kod žena iza raka dojke i pluća (1).

Opterećenje kolorektalnim karcinomom je najveće u Aziji, gde se godišnje zabeleži više od polovine svih novootkrivenih i umrlih slučajeva (2). U Kini se godišnje dijagnostikuje više od pola miliona novoobolelih od kolorektalnog karcinoma, a umre oko 280.000 ljudi (2). Međunarodna agencija za istraživanje raka (engl. *International Agency for Research on Cancer* – IARC) procenjuje da će globalno opterećenje kolorektalnim karcinomom porasti za 56% u periodu 2020-2040. godine, na više od 3 miliona novih slučajeva godišnje. Procenjeno povećanje broja smrtnih slučajeva od ove bolesti je još veće, i iznoi 69%, odnosno oko 1,6 miliona smrtnih slučajeva u svetu u 2040. godini. Očekuje se da će do najvećeg povećanja doći u zemljama sa visokim indeksom razvoja.

Dokazano je da različiti faktori mogu povećati ili smanjiti rizik od razvoja kolorektalnog karcinoma. Osim toga, većina ovih faktora utiče i na rizik od razvoja drugih malignih bolesti (2). Konzumiranje alkohola bilo je odgovorno za više od 160.000 novih slučajeva raka kolorektuma u 2020. godini, odnosno 8% svih slučajeva dijagnostikovanih te godine. Konzumiranje alkohola takođe povećava rizik za nastanak najmanje još šest drugih vrsta raka, uključujući rak jetre i rak dojke. Drugi poznati faktori rizika od raka uključuju pušenje i infekciju humanim papiloma virusom. Još jedan faktor koji povećava rizik od razvoja kolorektalnog karcinoma je gojaznost (2). Gojaznost je bila odgovorna za više od 85.000 slučajeva raka kolorektuma dijagnostikovanih 2020. godine, ili oko 4,4% svih slučajeva raka kolorektuma dijagnostikovanih te godine (3). Gojaznost takođe povećava rizik osobe da razvije najmanje još sedam drugih vrsta raka.

Cilj ove deskriptivne studije je bio da se analizira kretanje obolevanja i umiranja od kolorektalnog karcinoma kod muškaraca i žena Centralne Srbije u periodu od 1999. do 2020. godine.

Metode

Podaci o obolelima i umrlima od kolorektalnog karcinoma (šifre C18-C20 prema Internacionalnoj klasifikaciji bolesti), kao i o broju stanovnika, po polu i uzrastu, za period od 1999. do 2015. godine, preuzeti su iz registara za rak u Centralnoj Srbiji Instituta za javno zdravlje Srbije „Dr Milan Jovanović Batut" (4). Za period 2016-2020. podaci o obolelima i umrlima od kolorektalnog karcinoma dobijeni su na zahtev od Instituta za javno zdravlje Srbije „Dr Milan Jovanović Batut". Broj obolelih i umrlih od kolorektalnog karcinoma za svaku godinu dobijen je sabiranjem obolelih i umrlih od karcinoma kolona (šifra C18), rektosigmoidnog prelaza (šifra C19) i rektuma (šifra C20).

Na osnovu dobijenih podataka izračunate su sirove, uzrasno specifične i standardizovane stope incidencije i mortaliteta za kolorektalni karcinom. Metodom direktne standardizacije izračunate su standardizovane stope incidencije i mortaliteta, a kao standardna populacija odabrana je *Segi*-ju (1960) (5).

U cilju analize kretanja standardizovanih stopa incidencije i mortaliteta od kolorektalnog karcinoma za period od 1999-2020. godine korišćena je *joinpoint* regresiona analiza (*Joinpoint Regression Program, Version 4.9.0.1. February, 2022; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute*), prema metodu *Kim et al*. (6).

Rezultati

Prosečno procentualno učešće obolelih od kolorektalnog karcinoma u strukturi obolevanja od svih malignih tumora u Centralnoj Srbiji, u periodu 1999–2020. godine, kod muškaraca iznosilo je 12,5% dok je kod žena iznosilo 9% (tabela 1). Procentualno učešće umrlih od kolorektalnog karcinoma u strukturi umiranja od svih malignih tumora iznosilo je 12% kod muškaraca, a 10,9% kod žena

U periodu od 1999. do 2020. godine u Centralnoj Srbiji godišnje je od kolorektalnog karcinoma prosečno obolevalo 1696 muškarca i 1112 žena, a umiralo je prosečno 990 muškaraca i 676 žena (Tabela 2). Muškarci su češće i obolevali i umirali od kolorektalnog karcinoma u odnosu na žene. Prosečna standardizovana stopa incidencije za navedeni period iznosila je 34,4/100.000 za muškarace i 19,5/100.000 za žene, a prosečna standardizovana stopa mortaliteta je bila 18,4/100.000 za muškarace i 10,1/100.000 za žene. Prosečna standardizovana stopa incidencije kod muškaraca bila je 1,76 puta veća nego kod žena, dok je stopa mortaliteta bila 1,82 puta veća kod muškaraca nego žena.

could greatly reduce dying from this tumor, today colorectal cancer presents the second leading cause of death among all malignant tumors in the world, after lung cancer, when both sexes are considered (1). However, it is the third leading cause of death in men, after lung and liver cancer, and in women, after breast and lung cancer (1).

The burden of colorectal cancer is greatest in Asia, where more than half of all new cases and deaths are recorded annually (2). In China, more than half a million new cases of colorectal cancer are diagnosed annually, and about 280,000 people die (2). The International Agency for Research on Cancer (IARC) estimates that the global burden of colorectal cancer will increase by 56% between 2020 and 2040, to more than 3 million new cases per year. The estimated increase in the number of deaths caused by this disease is even higher, amounting to 69% or about 1.6 million deaths in the world in 2040. It is expected that the highest increase will occur in countries with a high index of development.

It has been proven that different factors can increase or decrease the risk of developing colorectal cancer. In addition, most of these factors also affect the risk of developing other malignant diseases (2). Alcohol consumption was responsible for more than 160,000 new cases of colorectal cancer in 2020, that is, 8% of all cases diagnosed that year. Alcohol consumption also increases the risk of at least six other types of cancer, including liver cancer and breast cancer. Other known risk factors for cancer include smoking and human papillomavirus infection. Another factor that increases the risk of developing colorectal cancer is obesity (2). Obesity was responsible for more than 85,000 cases of colorectal cancer that were diagnosed in 2020, or about 4.4% of all cases of colorectal cancer that were diagnosed during that year (3). Obesity also increases the risk of developing at least seven other types of cancer.

The aim of this descriptive study was to analyze the trends in morbidity and mortality of colorectal cancer in men and women in Central Serbia from 1999 to 2020.

Methods

Data on new cases and deaths caused by colorectal cancer (codes C18-C20 according to the International Classification of Diseases), as well as on the number of inhabitants, by gender and age for the period 1999-2015, were taken from the registries for cancer of the Public Health Institute "Dr Milan Jovanovic Batut" for Central Serbia (4). For the period 2016-2020, data on new cases and deaths from colorectal cancer were obtained at the request of the Public Health Institute "Dr Milan Jovanovic Batut". The number of new cases and deaths from colorectal cancer for each year was obtained by adding the new cases and deaths from cancer of the colon (code C18), rectosigmoid transition (code C19) and rectum (code C20).

Raw, age-specific and standardized incidence and mortality rates for colorectal cancer were calculated based on the obtained data. Standardized incidence and mortality rates were calculated using the direct standardization method, while Segi's population was used as the standard population (1960) (5).

In order to analyze trends in standardized incidence and mortality rates of colorectal cancer for the period 1999-2020, jointpoint regression analysis was used according to the method of Kim et al. (Jointpoint Regression Program, Version 4.9.0.1. February, 2022; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute) (6).

Results

The average percentage share of people affected by colorectal cancer in the structure of all malignant tumors in Central Serbia, during the period 1999-2020, was 12.5% in men, and 9% in women (Table 1). The percentage share of deaths caused by colorectal cancer in the structure of deaths from all malignant tumors was 12% in men and 10.9% in women.

From 1999 to 2020, in Central Serbia, on average, 1696 men and 1112 women were affected by colorectal cancer annually, while 990 men and 676 women died (Table 2). Men got ill and died more frequently in comparison to women. The average standardized incidence rate for the given time period amounted to 34.4/100,000 for men and 19.5/100,000 for women, while the average standardized mortality rate was 18.4/100,000 for men and 10.1/100,000 for women. The average standardized incidence rate in men was 1.76 times higher than in women, while the mortality rate was 1.82 times higher in men than in women.

Tabela 1. Procentualno učešće novoobolelih i umrlih od kolorektalnog karcinoma (C18-C20) među novoobolelima i umrlima od svih malignih tumora u muškoj i ženskoj populaciji, Centralna Srbija, 1999–2020. godine

Godine	Procentualno učešće novoobolelih od kolorektalnog karcinoma među novoobolelima od svih malignih		Procentualno učešće umrlih od kolorektalnog karcinoma među umrlima od svih malignih tumora	
	Muškarci	Žene	Muškarci	Žene
1999	12,3	9,0	10,8	10,5
2000	11,2	8,1	11,6	10,8
2001	12,0	8,7	10,9	10,2
2002	12,8	9,2	11,7	10,8
2003	12,9	9,4	11,2	11,2
2004	12,4	9,5	11,5	10,8
2005	12,9	9,8	12,2	12,4
2006	11,5	8,6	11,6	11,6
2007	13,3	10,7	11,5	11,0
2008	14,4	8,7	11,9	11,9
2009	12,1	8,4	12,4	11,4
2010	14,3	10,7	12,4	11,0
2011	10,6	8,1	11,6	11,3
2012	12,4	8,5	13,0	11,2
2013	12,8	9,0	13,2	10,6
2014	11,9	8,9	12,0	10,5
2015	13,4	9,4	12,7	10,8
2016	12,3	8,1	12,6	10,1
2017	11,8	8,0	12,7	10,1
2018	12,7	8,9	12,2	10,3
2019	12,0	8,8	12,6	10,4
2020	12,7	9,7	12,7	10,1
1999-2020	12,5	9,0	12,0	10,9

Prosečne uzrasno specifične stope incidencije od kolorektalnog karcinoma rastu sa godinama starosti kod oba pola. Najviše stope incidencije kod oba pola su zabeležene za uzrast 70 i više godina (262,1/100.000 muškaraca i 126/100.000 žena) (Tabela 3).

Kada se posmatraju uzrasno specifične stope incidencije od kolorektalnog karcinoma kod muškaraca značajan porast je zabeležen u uzrastu 60-69 godina od 1,7% godišnje i u uzrastu od 70 i više godina od 0,9 % godišnje. Kada se posmatraju svi uzrasti zajedno, standardizovana stopa incidencije značajno raste za 1% godišnje (Tabela 3, Grafikon 1). Kod žena uzrasta 50-59 godina zabeležen je značajan porast od 1% godišnje, a u uzrastu 60-69 godina porast od 1,4% godišnje. Standardizovane stope incidencije kod žena svih uzrasta su značajno rasle za 0,7% godišnje u periodu 1999-2020. godine.

Umiranje od kolorektalnog karcinoma je retko pre 30 godine kod oba pola, a zatim prosečne uzrasno specifične stope mortaliteta rastu su sa godinama starosti i najviše su kod osoba starih 70 i više godina (200,7/100.000 kod muškaraca i 106,0/100.000 kod žena) (Tabela 4). U svim uzrasnim grupama stope mortaliteta kod muškaraca su veće nego kod žena.

Kod muškaraca uzrasta 60-69 godina zabeležen je značajan godišnji porast stopa mortaliteta od 0,8% godišnje, a u uzrastu 70 i više godina značajan porast od 2,3% godišnje za period 1999-2013., a potom pad od 1,2% godišnje, ali bez značajnosti. Standardizovane stope mortlaliteta kod muškaraca bile su u značajnom porastu od 1,8% godišnje u

Table 1. Percent share of new cases and deaths from colorectal cancer (C18-C20) among new cases and deaths from all malignant tumors in the male and female population, Central Serbia, 1999–2020

Godine	Percent number of new cases of colorectal cancer of all malignant tumors		Percent number of deaths from colorectal cancer of all malignant tumors	
	Men	Women	Men	Women
1999	12.3	9.0	10.8	10.5
2000	11.2	8.1	11.6	10.8
2001	12.0	8.7	10.9	10.2
2002	12.8	9.2	11.7	10.8
2003	12.9	9.4	11.2	11.2
2004	12.4	9.5	11.5	10.8
2005	12.9	9.8	12.2	12.4
2006	11.5	8.6	11.6	11.6
2007	13.3	10.7	11.5	11.0
2008	14.4	8.7	11.9	11.9
2009	12.1	8.4	12.4	11.4
2010	14.3	10.7	12.4	11.0
2011	10.6	8.1	11.6	11.3
2012	12.4	8.5	13.0	11.2
2013	12.8	9.0	13.2	10.6
2014	11.9	8.9	12.0	10.5
2015	13.4	9.4	12.7	10.8
2016	12.3	8.1	12.6	10.1
2017	11.8	8.0	12.7	10.1
2018	12.7	8.9	12.2	10.3
2019	12.0	8.8	12.6	10.4
2020	12.7	9.7	12.7	10.1
1999-2020	12.5	9.0	12.0	10.9

The average age-specific incidence rates of colorectal cancer increased with age in both sexes. Both in men and women, the highest incidence rates were registered in the age group 70 years and older (262.1/100,000 men and 126/100,000 women) (Table 3).

Considering the age-specific incidence rates of colorectal cancer in men, a significant increase of 1.7% per year was registered in the age group 60-69 years and 0.9% in the age group 70 years and older. When all age groups are considered together, the standardized incidence rate increased significantly by 1% annually (Table 3, Figure 1). In women aged 50-59 years, a significant increase of 1% per year was registered, and 1.4% per year in the age group 60-69 years. Standardized incidence rates in women of all ages increased significantly by 0.7% per year in the period 1999-2020.

Dying from colorectal cancer is rare before the age of 30 among both sexes and then the average age-specific mortality rates increase with age and are the highest in people aged 70 years and older (200.7/100,000 in men and 106.0/100,000 in women) (Table 4). In all age groups, mortality rates in men are higher than in women.

Among men aged 60-69 years, a significant annual increase in the mortality rate of 0.8% per year was recorded, and in those aged 70 years and older, a significant increase of 2.4% per year for the period 1999-2013, and then a decrease of 1.2% per year, but without significance. Standardized mortality rates in men increased significantly by 1.8% per year in 1999-2010, then decreased by 1.2% (Table 4, Figure 2). In women aged 70 years and older, a significant increase of 2.4% per year was recorded from 1999 to 2008, and then there

Tabela 2. Broj novoobolelih i umrlih, standardizovane stope incidencije i mortaliteta (na 100.000 stanovnika) kolorektalnog karcinoma (C18-C20) po polu, Centralna Srbija, 1999–2020. godine

Godine	Muškarci				Žene			
	Number of new cases	Inc	Number of deaths	Mt	Number of new cases	Inc	Number of deaths	Mt
1999	1225	26,6	751	15,8	870	16,0	561	9,7
2000	1265	27,9	834	17,7	876	16,2	588	9,7
2001	1456	31,6	780	15,9	975	18,1	566	9,2
2002	1599	33,3	879	17,2	1053	18,9	602	9,2
2003	1591	33,6	855	17,2	1094	19,4	654	10,5
2004	1590	33,2	887	17,7	1135	20,5	647	10,2
2005	1635	34,4	957	18,7	1147	20,2	759	11,6
2006	1479	31,2	925	17,9	1007	17,8	712	11,0
2007	1788	37,8	950	17,9	1305	22,6	667	9,8
2008	1907	39,5	995	19,0	1046	18,2	753	11,4
2009	1693	35,7	1054	19,8	1057	19,2	743	10,9
2010	1943	40,4	1066	20,1	1342	24,7	711	10,5
2011	1502	30,3	994	18,6	1044	18,2	718	11,0
2012	1721	34,6	1134	20,1	1052	18,2	732	10,5
2013	1746	33,6	1131	19,9	1116	18,3	680	9,7
2014	1635	31,4	1028	18,3	1123	18,6	696	10,1
2015	1947	36,9	1120	19,7	1244	20,7	696	9,9
2016	1852	35,4	1100	18,9	1104	18,8	662	9,5
2017	1820	35,3	1111	19,3	1105	18,4	680	9,0
2018	2004	38,6	1066	18,7	1230	21,7	698	9,7
2019	1918	36,9	1094	18,7	1223	21,4	690	9,9
2020	1985	38,4	1057	18,1	1312	22,3	652	9,3
1999-2020	1696	34,4	990	18,4	1112	19,5	676	10,1

Inc–standardizovana stopa incidencije prema populaciji sveta (na 100.000 stanovnika); Mt–standardizovana stopa mortaliteta prema populaciji sveta (na 100.000 stanovnika)

periodu 1999-2010. godine, a potom sledi pad za 1,2% (Tabela 4, Grafikon 2). Kod žena uzrasta 70 i više godina zabeležen je značajan porast od 2,4% godišnje od 1999-2008, a potom u periodu 2008-2020. dolazi do značajnog pada od 1,5% godišnje. Kada se posmatraju standardizovane stope kod žena uočava se značajan trend porasta mortaliteta od 2,6% godišnje u periodu 1999-2006. godine, a potom pad od 1,2% godišnje za period 2006-2020.

Diskusija

U periodu od 1999. do 2020. godine u Centralnoj Srbiji je od kolorektalnog karcinoma prosečno obolevalo 1696 muškarca i 1112 žena godišnje. Muškarci su češće obolevali od kolorektalnog karcinoma u odnosu na žene. Prosečna standardizovana stopa incidencije za navedeni period iznosila je 34,4/100.000 kod muškaraca i 19,5/100.000 kod žena. Stope incidencije kolorektalnog karcinoma rastu sa godinama starosti kod oba pola.

Stope incidencije i mortaliteta od kolorektalnog karcinoma variraju širom sveta. Kolorektalni karcinom je češći kod muškaraca nego kod žena i 3-4 puta češći u razvijenim nego u zemljama u razvoju (6). U zemljama koje prolaze kroz tranziciju, stope incidencije imaju tendenciju da ravnomerno rastu sa povećanjem stepena razvoja, što ukazuje na uzročnu povezanost. Najviše stope incidencije su u razvijenim zemljama. U 2020. godini najviše stope incidencije zabeležene su u zemljama Evrope, Australiji i Novom Zelandu, dok najniže stope incidencije imaju zemlje Afrike i Centralne i Južne Azije.

Standardizovana stopa incidencije za karcinom kolorektuma u svetu u 2020. godini iznosi-

Table 2. The number of new cases and deaths, standardized incidence and mortality rates (per 100,000) caused by colorectal cancer (C18-C20) by sex, Central Serbia, 1999–2020

Years	Men				Women			
	Number of new cases	Inc	Number of deaths	Mt	Number of new cases	Inc	Number of deaths	Mt
1999	1225	26.6	751	15.8	870	16.0	561	9.7
2000	1265	27.9	834	17.7	876	16.2	588	9.7
2001	1456	31.6	780	15.9	975	18.1	566	9.2
2002	1599	33.3	879	17.2	1053	18.9	602	9.2
2003	1591	33.6	855	17.2	1094	19.4	654	10.5
2004	1590	33.2	887	17.7	1135	20.5	647	10.2
2005	1635	34.4	957	18.7	1147	20.2	759	11.6
2006	1479	31.2	925	17.9	1007	17.8	712	11.0
2007	1788	37.8	950	17.9	1305	22.6	667	9.8
2008	1907	39.5	995	19.0	1046	18.2	753	11.4
2009	1693	35.7	1054	19.8	1057	19.2	743	10.9
2010	1943	40.4	1066	20.1	1342	24.7	711	10.5
2011	1502	30.3	994	18.6	1044	18.2	718	11.0
2012	1721	34.6	1134	201	1052	18.2	732	10.5
2013	1746	33.6	1131	19.9	1116	18.3	680	9.7
2014	1635	31.4	1028	18.3	1123	18.6	696	10.1
2015	1947	36.9	1120	19.7	1244	20.7	696	9.9
2016	1852	35.4	1100	18.9	1104	18.8	662	9.5
2017	1820	35.3	1111	19.3	1105	18.4	680	9.0
2018	2004	38.6	1066	18.7	1230	21.7	698	9.7
2019	1918	36.9	1094	18.7	1223	21.4	690	9.9
2020	1985	38.4	1057	18.1	1312	22.3	652	9.3
1999-2020	1696	34.4	990	18.4	1112	19.5	676	10.1

Inc–standardized incidence rate according to the world population (per 100,000); Mt–standardized mortality rate according to the world population (per 100,000)

was a significant decrease of 1.5% per year. When standardized rates in women are observed, a significant trend of increase in mortality of 2.6% per year was noticed in the period 1999-2006, and then a decrease of 1.2% per year in the period 2006-2020.

Discussion

In the period 1999-2020, an average of 1,696 men and 1,112 women fell ill with colorectal cancer per year in Central Serbia. Men suffered from colorectal cancer more often than women. The average standardized incidence rate for the mentioned period was 34.4/100,000 in men and 19.5/100,000 in women. Incidence rates of colorectal cancer increase with age in both men and women.

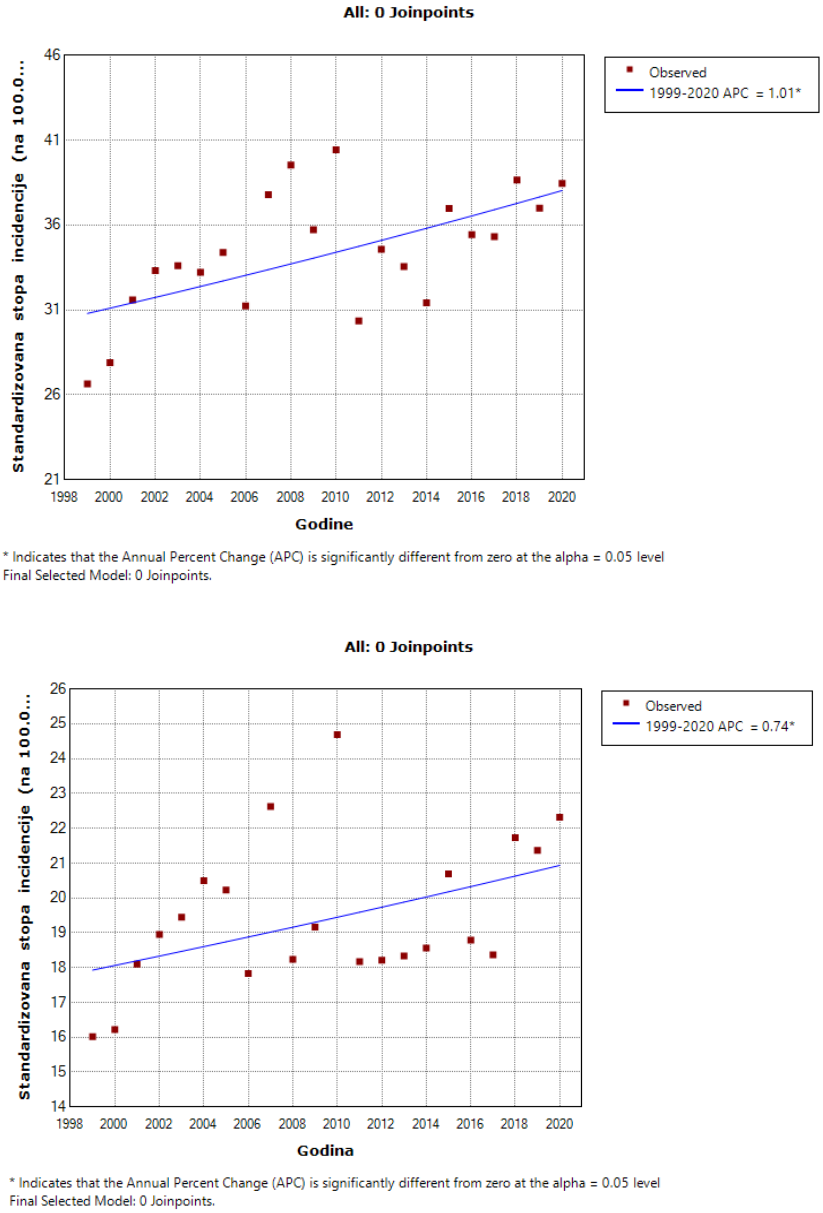
Incidence and mortality rates of colorectal cancer vary worldwide. Colorectal cancer is more common in men than women and 3-4 times more common in developed than developing countries (7). In transition countries, incidence rates tend to rise steadily with increasing levels of development, suggesting a causal relationship. The highest incidence rates are in developed countries. In 2020, the highest incidence rates were registered in European countries, Australia and New Zealand, while the lowest incidence rates were found in the countries of Africa and Central and South Asia.

The standardized incidence rate for colorectal cancer in the world in 2020 was 19.5/100,000 (1). In 2020, as far as both sexes are concerned, Hungary had the highest standardized incidence rate of colorectal cancer in Europe, and also in

Tabela 3. Prosečne uzrasno-specifične i standardizovane stope incidencije (na 100.000), *joinpoint* analiza kretanja stopa incidencije kolorektalnog karcinoma (C18-C20) po polu, Centralna Srbija, period 1999-2020. godina

	Muškarci			Žene		
Uzrasne grupe	**Inc**	**Period**	**APC (95%IP)**	**Inc**	**Period**	**APC (95%IP)**
< 30	0,7	1999-2008 2008-2020	12 (-1,1 – 26,9) -9,3* (-16,3- -1,6)	0,6	1999-2020	-1,9 (-5,9 – 2,2)
30-39	6,5	1999-2020	-1,8 (-4,4 – 1,0)	5,5	1999-2020	0,1 (-2,2 – 2,5)
40-49	23,0	1999-2020	-0,9 (-2,1 – 0,3)	19,4	1999-2020	-0,2 (-1,5 – 1,1)
50-59	80,3	1999-2020	1,7 (-0,5 – 3,9)	51,7	1999-2020	1,0* (0,3 – 1,7)
60-69	186,7	1999-2020	1,7* (0,8 – 2,5)	95,6	1999-2020	1,4* (0,5 – 2,3)
70+	262,2	1999-2020	0,9* (0,3 – 1,5)	126,0	1999-2020	0,0 (-0,7 – 0,6)
Stand. stope	34,4	1999-2020	1,0* (0,4 – 1,6)	19,5	1999-2020	0,7* (0,1 – 1,4)

Inc – Stope incidencije; ** Standardizovane stope prema populaciji sveta (na 100.000); APC –Annual Percent Change – prosečna procentualna godišnja promena; 95%IP- 95% interval poverenja; *-APC je značajno različit od 0 za alfa=0,05

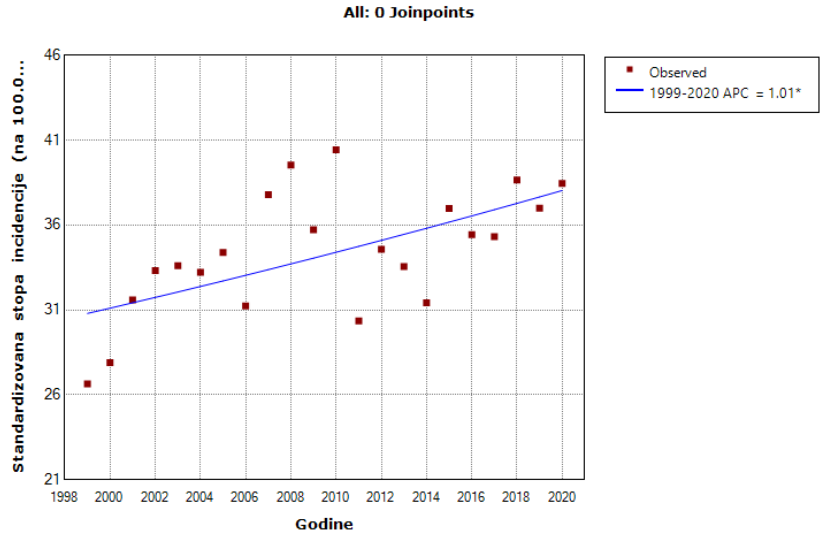


Grafikon 1. *Joinpoint* analiza kretanja stopa incidencije kolorektalnog karcinoma (C18-C20) po polu, Centralna Srbija, period 1999-2020. godine (a) muškarci, b) žene

Table 3. Average age-specific and standardized incidence rates (per 100,000), joinpoint regression analysis of trends in incidence of colorectal cancer (C18-C20) by sex, Central Serbia, 1999-2020

	Men			Women		
Age groups	**Inc**	**Period**	**APC (95%CI)**	**Inc**	**Period**	**APC (95%CI)**
< 30	0.7	1999-2008 2008-2020	12 (-1.1 – 26.9) -9.3* (-16.3- -1.6)	0.6	1999-2020	-1.9 (-5.9 – 2.2)
30-39	6.5	1999-2020	-1.8 (-4.4 – 1.0)	5.5	1999-2020	0.1 (-2.2 – 2.5)
40-49	23.0	1999-2020	-0.9 (-2.1 – 0.3)	19.4	1999-2020	-0.2 (-1.5 – 1.1)
50-59	80.3	1999-2020	1.7 (-0.5 – 3.9)	51.7	1999-2020	1.0* (0.3 – 1.7)
60-69	186.7	1999-2020	1.7* (0.8 – 2.5)	95.6	1999-2020	1.4* (0.5 – 2.3)
70+	262.2	1999-2020	0.9* (0.3 – 1.5)	126.0	1999-2020	0.0 (-0.7 – 0.6)
Stand. rates**	34.4	1999-2020	1.0* (0.4 – 1.6)	19.5	1999-2020	0.7* (0.1 – 1.4)

Inc–Incidence rates;**Standardized rates according to the world population (per 100,000); APC –Annual Percent Change; 95%CI-95% confidence interval;*-APC is significantly different from 0 at the alpha=0.05



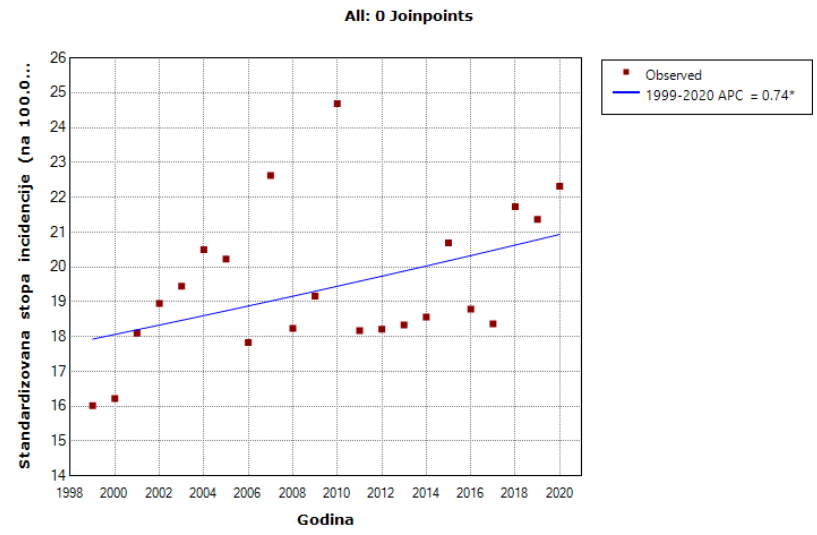
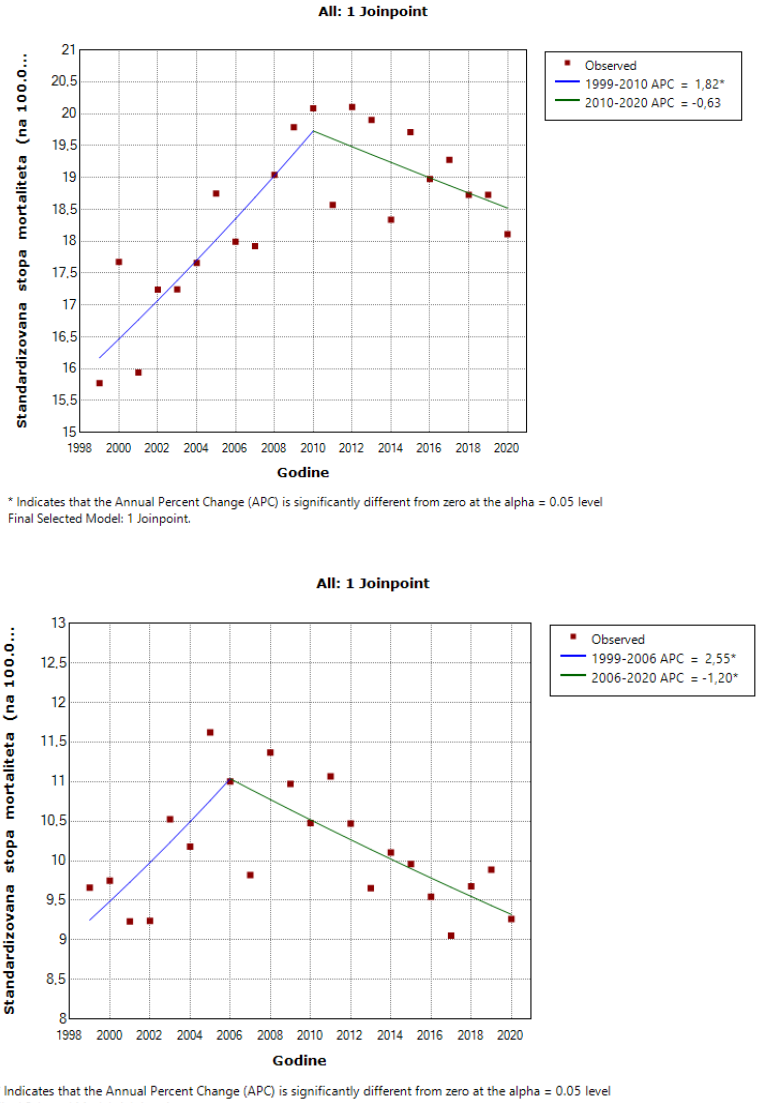


Figure 1. Jointpoint analysis of trends in incidence rates of colorectal cancer (C18-C20) by sex, Central Serbia, period 1999-2020, a) men, b) women

Tabela 4. Prosečne uzrasno-specifične i standardizovane stope incidencije (na 100.000), *joinpoint* analiza kretanja stopa mortaliteta kolorektalnog karcinoma (C18-C20) po polu, Centralna Srbija, period 1999-2020. godina

	Muškarci			Žene		
Uzrasne grupe	**Mt**	**Period**	**APC (95%IP)**	**Mt**	**Period**	**APC (95%IP)**
< 30	0,2	1999-2020	-	0,2	1999-2020	-
30-39	2,1	1999-2020	-1,1 (-3,8 – 1,8)	1,9	1999-2020	1,9 (-0,3 – 4,1)
40-49	9,2	1999-2020	-0.4 (-1.9 – 1.1)	6,9	1999-2020	-1,1 (-2,3 – 0,0)
50-59	31,9	1999-2010 2010-2020	2,4* (0,3 – 4,7) -2,7* (-5,1 – -0,2)	20,2	1999-2020	0,3 (-0,9 – 1,5)
60-69	92,1	1999-2020	0,8* (0,3 – 1,3)	46,1	1999-2020	-0,2 (-0,9 – 0,5)
70+	200,7	1999-2013 2013-2020	2,3* (1,7 – 3,0) -1,3 (-3,0 – 0,5)	106,0	1999-2008 2008-2020	2,4* (0,9 – 4,0) -1.5* (-2,4--0,5)
Stand. stope**	18,4	1999-2010 2010-2020	1,8* (1,1 – 2,6) -1,2 (-0,6 – -1,4)	10,1	1999-2006 2006-2020	2,6* (0,4 – 4,7) -1,2*(-1.9 – -0,5)

Mt – Stope mortaliteta; **Standardizovane stope prema populaciji sveta (na 100.000); APC –Annual Percent Change – prosečna procentualna godišnja promena; 95%IP- 95% interval poverenja; *-APC je značajno različit od 0 za alfa=0,05



Grafikon 2. *Joinpoint* analiza kretanja stopa mortaliteta kolorektalnog karcinoma po polu, Centralna Srbija, period 1999-2020. godina, a) muškarci, b) žene

Table 4. Average age-specific and standardized mortality rates (per 100,000), joinpoint analysis of trends in mortality rates of colorectal cancer by sex, Central Serbia, period 1999-2020

	Men			Women		
Age groups	**Mt**	**Period**	**APC (95%CI)**	**Mt**	**Period**	**APC (95%CI)**
< 30	0.2	1999-2020	-	0.2	1999-2020	-
30-39	2.1	1999-2020	-1.1 (-3.8 – 1.8)	1.9	1999-2020	1.9 (-0.3 – 4.1)
40-49	9.2	1999-2020	-0.4 (-1.9 – 1.1)	6.9	1999-2020	-1.1 (-2.3 – 0.0)
50-59	31.9	1999-2010 2010-2020	2.4* (0.3 – 4.7) -2.7* (-5.1 – -0.2)	20.2	1999-2020	0.3 (-0.9 – 1.5)
60-69	92.1	1999-2020	0.8* (0.3 – 1.3)	46.1	1999-2020	-0.2 (-0.9 – 0.5)
70+	200.7	1999-2013 2013-2020	2.3* (1.7 – 3.0) -1.3 (-3.0 – 0.5)	106.0	1999-2008 2008-2020	2.4* (0.9 – 4.0) -1.5* (-2.4--0.5)
Stand. rates**	18.4	1999-2010 2010-2020	1.8* (1.1 – 2.6) -1.2 (-0.6 – -1.4)	10.1	1999-2006 2006-2020	2.6* (0.4 – 4.7) -1.2*(-1.9 – -0.5)

Mt–mortality rates; ** Standardized mortality rates according to the world population (per 100,000); APC – Annual Percent Change; 95%CI-95% confidence interval;*-APC is significantly different from zero at alpha=0,05

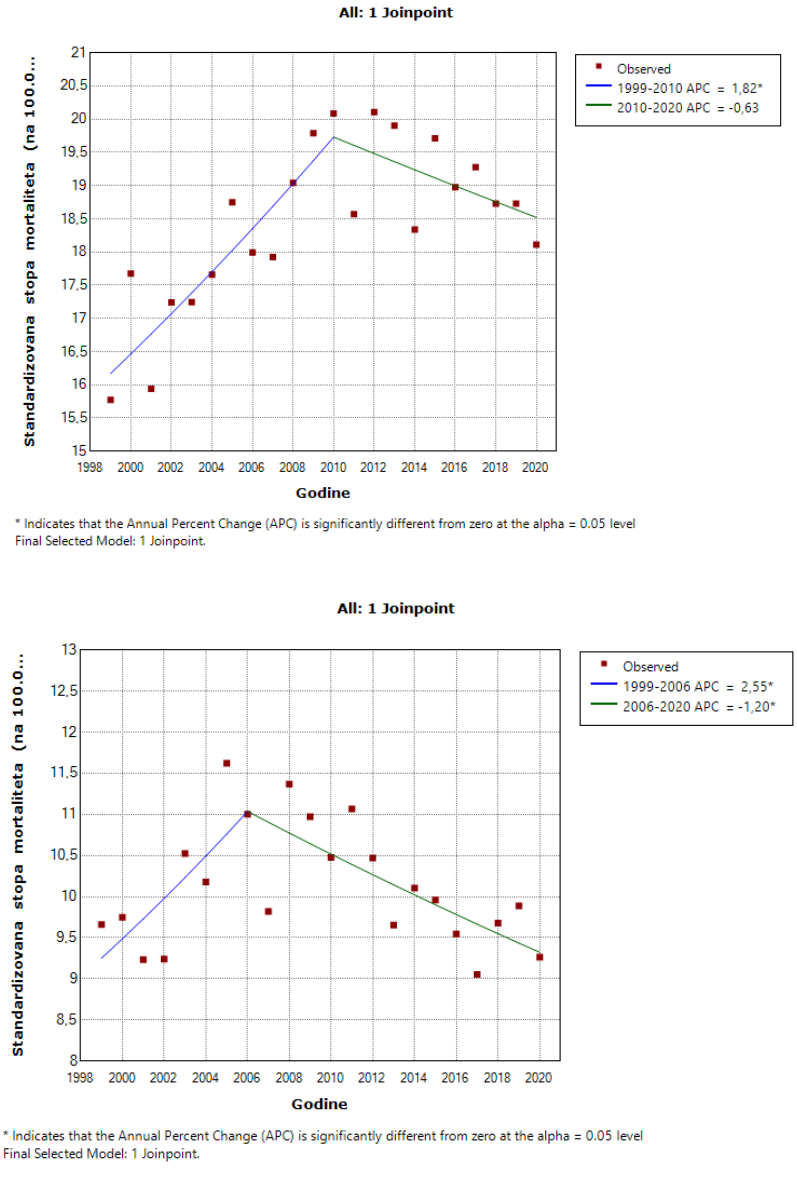


Figure 2. Joinpoint analysis of trends in mortality rates of colorectal cancer by sex, Central Serbia, period 1999-2020, a) men, b) women

la je 19,5/100.000 (1). Posmatrano za oba pola u 2020. godini Mađarska je imala najveću standardizovanu stopu incidencije kolorektalnog karcinoma u Evropi, ali i u svetu, (45,3/100.000), zatim Slovačka (43,9/100.000), Norveška (41,9/100.000), Holandija (41/100.000) i Danska (40,9/100.000) (1). Ako se posmatra samo muški pol za istu godinu situacija je slična, na prvom mestu je Mađarska (62/100.000), zatim Slovačka (60,7/100.000), Slovenija (55,8/100.000) i Portugal (55,2/100.000) (1). Kod ženskog pola najveću standardizovanu stopu incidencije 2020. imala je Norveška (38,7/100.000), potom Danska (35,6/100.000), Holandija (34,3/100.000) i Mađarska (33,1/100.000). Zemlje sa najmanjim stopama incidencije ovog tumora za oba pola u 2020. godini (<6,7/100.000) bile su Indija, Pakistan, Avganistan, i zemlje Afričkog kontinenta. U Evropi, najmanje stope incidencije zabeležene su u Albaniji (7,7/100.000), Austriji (21,0/100.000) i Švajcarskoj (22,3/100.000)

Trendovi incidencije i mortaliteta od kolorektalnog karcinoma u svetu mogu se podeliti u tri različite kategorije. Prva kategorija, koju čine srednje razvijene zemlje, kao što su Brazil, Rusija, Kina, Latinska Amerika, i Baltičke zemlje. Ove zemlje prolaze kroz ekonomsku tranziciju, što je verovatno uzrok povećanja obolevanja. Druga kategorija, koju čine uglavnom visoko razvijene zemlje kao što su Kanada, Velika Britanija, Danska i Singapur beleže porast incidencije, ali pad mortaliteta, zbog poboljšanja mogućnosti lečenja. Na kraju, treću kategoriju čine zemlje sa najvišim stepenom razvoja, kao što su Sjedinjene Američke Države, Island, Japan, i Francuska koje beleže pad incidencije i mortaliteta zbog napretka u prevenciji i lečenju (7,8). Zabeleženi padovi mortaliteta mogu se povezati sa povećanim preživljavanjem usled razvoja i primene savremenijih načina lečenja ovog tumora. Takođe, uklanjanje polipa i rana detekcija prekanceroznih i kanceroznih lezija pomoću metoda skrininga igraju značajnu ulogu. Uvođenje programa skrininga u početku dovodi do porasta stopa incidencije jer se diganostikuju prethodno neprepoznate bolesti, ali posmatrano u dužem periodu smanjuju mortlitet zahvaljujući uklanjanju promena (8)

U periodu 1999-2020. godine, u Centralnoj Srbiji standardizovane stope incidencije kolorektalnog karcinoma značajno rastu, i to za 0,7% godišnje za žene i 1% godišnje za muškarce. Prema podacima American Cancer Society stope incidencije pokazuju porast od 1975. i tokom osamdesetih godina prošlog veka, nakon čega se uočava njihov pad (9). U SAD poslednjih decenija beleži se pad stopa incidencije kolorektalnog karcinoma kod starijih od 50 godina, dok je primećen porast incidencije kod osoba uzrasta 20 do 49 (7). Stopa incidencije kolorektalnog karcinoma za uzrast 20-49 godina bila je 9,3/100.000 1975. godine dok je u 2015. godini iznosila 13,7/100.000 (porast od 47,31%), dok su stope incidencije u uzrasnoj grupi 50 i više godina u stalnom padu. U SAD u periodu 2000-2020. godina, stope incidencije u periodu 2000-2007. opadaju za 2,4% godišnje, 2007-2012. za 3,4% godišnje, da bi potom u periodu 2012-2020. pad bio svega 0,9% godišnje (10). Smjanjenje incidencije u ranim 2000. pripisuje se podjednako smanjenoj učestalosti faktora rizika i povećanom skriningu (9). Sa druge strane, pad trenda u kasnim 2000. godinama se prvenstveno pripisuje velikom obuhvatu skrininga kolonoskopijom u starosnoj grupi 50+, koji je sa 20% u 2000. godini porastao na 61% u 2018. godini (11). Pokazalo se da uvođenje skrining programa u početku dovodi do povećanja incidencije usled detekcije nedijagnostikovanih obolenja, ali dugoročno dovodi do pada u incidenciji zbog sve češćeg otkrivanja prekanceroznih lezija (12).

Procenjuje se da će do 2040. godine broj slučajeva kolorektalnog karcinoma u svetu porasti na više od 3 miliona novih slučajeva godišnje i oko 1,6 miliona smrtnih slučajeva (2). Ovakav porast se očekuje usled eknomskog napredovanja slabije i srednje razvijenih država, kao i preovladavnja faktora rizika u tim populacijama. Neki od faktora rizika su: fizička neaktivnost, alkohol, pušenje, hrana bogata životinjskim mastima i crvenim mesom, gojaznost itd. (7).

U 2020. godini najviše stope mortaliteta od raka kolorektuma zabeležene su u Australiji i Novom Zelandu, Evropskim zemljama, dok najniže stope incidencije imaju zemlje Afrike i Centralne i Južne Azije. Prosečna standardizovana stopa mortaliteta u svetu iznosila je 9/100.000. Najveća standardizovana stopa mortaliteta za oba pola u 2020. bila je u Slovačkoj (21/100.000), zatim Mađarskoj (20,2/100.000), Hrvatskoj (19,6/100.000) itd (1). Ako se posmatra samo muški pol vodeće zemlje su Slovačka (29,6/100.000), Mađarska (29/100.000), Hrvatska (28,2/100.000), Moldavija (26,7/100.000), a za žene to su Slovačka (14,8/100.000), Mađarska (14/100.000), Hrvatska (13,5/100.000), Singapur (12,8/100.000). Države sa

the world (45.3/100,000), followed by Slovakia (60.7/100,000), Slovenia (55.8/100,000), Norway (41.9/100,000), the Netherlands (41/100,000) and Denmark (40.9/100,000) (1). If only the male sex is observed for the same year, the situation is similar, that is, Hungary is in the first place (62/100,000), followed by Slovakia (60.7/100,000), Slovenia (55.8/100,000) and Portugal (55.2/100,000) (1). In women, the highest standardized incidence rate in 2020 was in Norway (38.7/100,000), followed by Denmark (35.6/100,000), the Netherlands (34.3/100,000) and Hungary (33.1/100,000). In 2020, the countries with the lowest incidence rates of this tumor for both sexes (<6.7/100,000) were India, Pakistan, Afghanistan and the countries of the African continent. In Europe, the lowest incidence rates were registered in Albania (7.7/100,000), Austria (21.0/100,000) and Switzerland (22.3/100,000).

In the world, the trends in incidence and mortality of colorectal cancer can be divided into three different categories. The first category, which consists of moderately developed countries, such as Brazil, Russia, China, Latin America and the Baltic countries. These countries are going through economic transition, which is probably the cause of the increase in morbidity. The second category, which consists mainly of highly developed countries such as Canada, Great Britain, Denmark and Singapore, recorded an increase in incidence, but a decrease in mortality, due to improved treatment options. Finally, the third category consists of countries with the highest level of development, such as the United States of America, Iceland, Japan, and France, which record a decrease in incidence and mortality due to improved prevention and treatment (7,8). The decrease in mortality can be associated with the increased survival due to the development and application of contemporary methods of treatment of this tumor. Also, removing polyps and early detection of precancerous and cancerous lesions with the help of screening methods have an important role. The introduction of screening programs initially leads to an increase in incidence rates because previously unrecognized diseases are diagnosed, but when observed in the long term, they reduce mortality because changes are removed (8).

In the period 1999-2020, in Central Serbia, standardized incidence rates of colorectal cancer increased significantly, by 0.7% per year for women and 1% per year for men. According to the data of the American Cancer Society, incidence rates showed an increase since 1975 and during the 1980s, and after that their decrease was observed (9). In the last decades, in the USA, incidence rates of colorectal cancer decreased in people older than 50, while the increase in incidence was observed in people aged 20 to 49 years (7). The incidence rate of colorectal cancer in the age group 20-49 years was 9.3/100,000 in 1975, while in 2015 it amounted to 13.7/100,000 (increase of 47.31%), while the incidence rates in the age group 50 years and older constantly decreased. In the period 2000-2020, in the USA, incidence rates in the period 2000-2007 decreased by 2.4% per year, and in the period 2007-2012 by 3.4% per year, while in the time period 2012-2020, the decline was only 0.9 per year (10). The decrease in incidence in the early 2000s was attributed equally to a reduced frequency of risk factors and increased screening (9). On the other hand, the trend of decline in the late 2000s was primarily attributed to the high coverage of colonoscopy screening in the age group 50+, which increased from 20% in 2000 to 61% in 2018 (11). It was shown that the introduction of screening programs initially led to an increase in incidence because undiagnosed diseases were detected, but in the long term, it led to a decrease in incidence due to the more frequent detection of precancerous lesions (12).

It is estimated that by 2040, the number of colorectal cancer cases worldwide will increase to more than 3 million new cases per year and about 1.6 million deaths (2). This increase is expected due to the economic progress of less and moderately developed countries, as well as due to the prevalence of risk factors in these populations. Some of the risk factors are: physical inactivity, alcohol, smoking, food rich in animal fat and red meat, obesity, etc. (7).

In 2020, the highest mortality rates of colorectal cancer were registered in Australia and New Zealand, European countries, while the lowest incidence rates were in the countries of Africa and Central and East Asia. The average standardized mortality rate in the world was 9/100,000. The highest standardized mortality rate for both sexes in 2020 was in Slovakia (21/100,000), followed by Hungary (20.2/100,000), Croatia (19.6/100,000), etc. (1). When only the male gender is observed,

najmanjim standardizovanim stopama mortaliteta za oba pola (<4,6/100.000) 2020. godine bile su Egipat, Sudan, Avganistan, Indija, Pakistan itd (1,3). Za muški pol to su bile Bolivija (3,9/100.000), Pakistan (3,5/100.000), Indija (3,6/100.000), Mongolija (4/100.000) (1,3). Kod žena je slična situacija: Indija (2,1/100.000), Pakistan (2,5/100.000), Sudan (3,6/100.000), Egipat (3,5/100.000) itd. U Centralnoj Srbiji, prosečna standardizovana stopa mortaliteta je bila 18,4/100.000 kod muškaraca i 10,1/100.000 kod žena.

U periodu 1999-2020. godine u Centralnoj Srbiji kod žena uočava se značajan trend porasta stopa mortaliteta kolorektalnog karcinoma od 2,6% godišnje u periodu 1999-2006. godine, a potom pad od 1,2% godišnje za period 2006-2020. Međutim, kod muškaraca se uočava značajan porast u periodu 1999-2010. za 1,8% godišnje, a zatim pad od -1,2% godišnje, ali pad nije bio značajan. Kod muškaraca uzrasta 60-69 godina zabeležen je značajan godišnji porast stopa mortaliteta od 0,8% godišnje za period 1999-2020., a u uzrastu 70 i više godina porast od 2,3% godišnje samo za period 1999-2013. godine. Trend porasta je prisutan i kod muškaraca uzrasta 50-59 godina u periodu 1999-2010. godine za 2,4% godišnje, a potom pad od 1,3% godišnje. Kod žena uzrasta 70 i više godina zabeležen je značajan porast stopa mortaliteta od 2,4% godišnje u periodu 1999-2008, a potom u periodu 2008-2020. dolazi do značajnog pada od 1,5% godišnje.

U SAD stope mortaliteta su se generalno smanjile od 1975. godine, najviši značajan pad je u starosnoj grupi od 75 i više godina (7). Povećanje mortaliteta beleži se u Latinskoj Americi, Karibima i Aziji (13,14). Ovo je posledica slabije razvijene zdravstvene zaštite u tim zemljama, kao i nedostupnosti adekvatnih metoda skrininga (15).

Kina je jedna od zemalja gde se godišnje beleže visoke stope mortaliteta. Kretanje stopa mortaliteta u ovoj državi pokazuje značajan porast od 4,1% godišnje u periodu 2002-2015. godina (16). Ubrzan privredno-ekonomski razvoj i sve više prihvatanje zapadnog načina života smatraju se glavnim uzrokom za primećeni porast. Ovo se poklapa sa podacima iz drugih država u razvoju kao što su zemlje Južne Amerike, Istočne Evrope i Rusija (8). Sa druge strane stope mortaliteta opadaju u razvijenim zemljama (8). Smatra se da je to posledica obuhvata velikog procenta populacije savremenim skrining metodama.

U Sjedinjenim Američkim Državama stope mortaliteta kolorektalnog karcinoma pokazuju pad kod žena još od 1947, a tek od 1980. kod muškaraca (11). Posmatrajući trendove mortaliteta u poslednje tri decenije nema velikih razlika po polu. Pad mortaliteta do 2000. godine pripisuje se poboljšanju u lečenju (12%), promeni u faktorima rizika (35%) i skriningu (53%).

Više od polovine svih slučajeva kolorektalnog karcinoma može se pripisati faktorima životnog stila, uključujući nezdravu ishranu, nedovoljnu fizičku aktivnost, prekomerno konzumiranje alkohola i pušenje (17). Ovakav životni stil se povezuje sa zemljama sa visokim prihodima, gde su stope incidencije kolorektalnog karcinom najviše (7). Na globalnom nivou, povećanje incidencije kolorektalnog karcinoma se smatra markerom ekonomske tranzicije. S druge strane brojne studije su pokazale da ljudi sa zdravim načinom života imaju 27% do 52% manji rizik od kolorektalnog karcinoma u poređenju sa onima koji ne vode zdrav stil života (18). Nepromenljivi faktori koji povećavaju rizik su genetski faktori i medicinska istorija, uključujući u ličnoj ili porodičnoj anamnezi kolorektalni karcinom ili adenoma i u ličnoj anamnezi dugotrajnu hroničnu inflamatornu bolesti creva. Većina ljudi sa povećanim rizikom zbog medicinske ili porodične istorije treba da počne sa skriningom na kolorektalni karcinom pre 45. godine (11). Smanjenje telesne težine, fizička aktivnost i dijeta bogata ribom, voćem i povrćem mogu smanjiti rizik od razvoja kolorektalnog karcinoma. Podvrgavanje organizovanim skrining programima povećava šansu za otkrivanje kolorektalnog karcinoma dok je u ranoj, i potencijalno lakšoj i izlečivoj fazi.

Zaključak

Trend porasta obolevanja od kolorektalnog karcinoma ukazuje na neophodno unapređenje sprovođenja organizovanog skrininga za kolorektalni karcinom u Centralnoj Srbiji, kao i na važnost sprovođenja edukacije stanovništva o faktorima rizika za nastanak ovog malignoma i mogućnostima prevencije. Poslednjih godina, kod oba pola, beleži se pad umiranja od kolorektalnog karcinoma, što govori o unapređenju dijagnostike i lečenja ovog malignoma.

Konflikt interesa

Autori su izjavili da nema konflikta interesa.

the leading countries were Slovakia (29.6/100,000), Hungary (29/100,000), Croatia (28.2/100,000), Moldova (26.7/100,000), and for women, the following countries: Slovakia (14.8/100,000), Hungary (14/100,000), Croatia (13.5/100,000), Singapore (12.8/100,000). In 2020, the countries with the lowest standardized mortality rates for both sexes (<4/6/100,000) were Egypt, Sudan, Afghanistan, India, Pakistan, etc. (1,3). In men, these countries were Bolivia (3.9/100,000), Pakistan (3.5/100,000), India (3.6/100,000), Mongolia (4/100,000) (1,3). In women, the situation was similar: India (2.1/100,000), Pakistan (2.5/100,000), Sudan (3.6/100,000), Egypt (3.5/100,000), etc. In Central Serbia, the average standardized mortality rate was 18.4/100,000 in men and 10.1/100,000 in women.

In the period 1999-2020, in Central Serbia in women, a significant trend of increase in the mortality rate of colorectal cancer of 2.6% per year was observed in the period 1999-2006, and then a decline of 1.2% per year in the period 2006-2020. However, in men, a significant increase can be observed in the period 1999-2010, by 1.8% per year and then a decline of -1.2% per year, but the decline was not significant. In men aged 60-69 years, a significant annual increase in the mortality rate of 0.8% per year was registered in the period 1999-2020, and in the age group 70 years and older, the increase of 2.3% per year was observed only in the period 1999-2013. The trend of increase of 2.4% per year was also present in men aged 50-59 in the period 1999-2010, followed by a decrease of 1.3% per year. In women aged 70 years and older, a significant increase in mortality rates of 2.4% per year was registered in the period 1999-2008, followed by a significant decrease of 1.5% per year in the period 2008-2020.

In the USA, mortality rates have generally declined since 1975, and the highest significant decline was in the age group 75 years and older (7). An increase in mortality was noted in Latin America, the Caribbean and Asia (13,14). This is the consequence of less developed health care in those countries, as well as the unavailability of adequate screening methods (15).

China is one of the countries where annual high mortality rates were recorded. The trends in mortality rates in this country showed a significant increase of 4.1% per year in the period 2002-2015 (16). Rapid socio-economic development and the increasing acceptance of the Western way of life are deemed to be the main reasons for the observed increase. This is in line with data from other developing countries, such as the countries of South America, Eastern Europe, and Russia (8). On the other hand, mortality rates are decreasing in developed countries (8). It is considered to be the consequence of great coverage of population with modern screening methods.

In the United States of America, mortality rates of colorectal cancer in women have decreased since 1947, and only since 1980 in men (11). Considering mortality trends in the last three decades, there has been no significant difference regarding gender. The decline in mortality by 2000 was attributed to the improvement in treatment (12%), changes in risk factors (35%) and screening (53%).

More than half of all cases of colorectal cancer can be attributed to lifestyle factors, including unhealthy diet, insufficient physical activity, excessive alcohol consumption, and smoking (17). This lifestyle is associated with high income countries, where the incidence rates of colorectal cancer are the highest (8). Globally, the increase in the incidence of colorectal cancer is considered to be the marker of economic transition. On the other hand, numerous studies have shown that people with a healthy lifestyle have a 27% to 52% lower risk of colorectal cancer compared to those who do not lead a healthy lifestyle (18). Non-modifiable factors that increase the risk are genetic factors and medical history, including colorectal cancer or adenoma in the personal or family history and a long term chronic inflammatory bowel disease in the personal medical history. The majority of people who are at an increased risk of colorectal cancer due to their medical or family history should start screening for CRC before the age of 45 (11). Weight loss, physical activity and diet rich in fish, fruit and vegetables can reduce the risk of developing colorectal cancer. Organized screening programs increase the chance of detecting colorectal cancer while it is in an early, potentially easier and curable stage.

Conclusion

The trend of increasing incidence of colorectal cancer points to the necessary improvement of organized screening for colorectal cancer in Central Serbia, as well as the importance of educating the population about the risk factors for the

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Reference

1. Cancer today [Internet]. [cited 2023 May 27]. Available from: http://gco.iarc.fr/today/home
2. Colorectal Cancer Awareness Month 2022 – IARC [Internet]. [cited 2023 May 27]. Available from: https://www.iarc.who.int/featured-news/colorectal-cancer-awareness-month-2022/
3. Cancer and obesity [Internet]. [cited 2023 May 27]. Available from: http://gco.iarc.fr/obesity/home
4. IZJZS - Batut: Publikacije [Internet]. [cited 2023 May 27]. Available from: https://www.batut.org.rs/index.php?category_id=9
5. Segi M. Cancer mortality for selected sites in 24 countries (1950-57). Sendai, Japan: Department of Public Health, Tohoku University of Medicine; 1960.
6. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3):335–51. doi: 10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z
7. Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Gastroenterol Rev. 2019;14(2):89–103. doi: doi: 10.5114/pg.2018.81072
8. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683–91. doi: doi: 10.1136/gutjnl-2015-310912.
9. Edwards BK, Ward E, Kohler BA, Eheman C, Zauber AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer. 2010;116(3):544–73. doi: doi: 10.1002/cncr.24760.
10. SEER*Explorer Application [Internet]. [cited 2023 Jun 1]. Available from: https://seer.cancer.gov/statistics-network/explorer/application.html
11. American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.
12. Levin B, Lieberman DA, McFarland B, Smith RA, Brooks D, Andrews KS, et al. Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology*†. CA Cancer J Clin. 2008;58(3):130–60. doi: 10.3322/CA.2007.0018
13. Chatenoud L, Bertuccio P, Bosetti C, Levi F, Curado MP, Malvezzi M, et al. Trends in cancer mortality in Brazil, 1980–2004. Eur J Cancer Prev. 2010;19(2):79.
14. Malvezzi M, Bosetti C, Chatenoud L, Rodríguez T, Levi F, Negri E, et al. Trends in cancer mortality in Mexico, 1970–1999. Ann Oncol. 2004;15(11):1712–8. doi: doi: 10.1093/annonc/mdh424.
15. Scaling up cancer diagnosis and treatment in developing countries: what can we learn from the HIV/AIDS epidemic? Ann Oncol. 2010;21(4):680–2. doi: doi: 10.1093/annonc/mdq055.
16. Yu W, Jiang J, Xie L, Li B, Luo H, Fu Y, et al. Mortality Trends in Colorectal Cancer in China During 2000–2015: A Joinpoint Regression and Age-Period-Cohort Analysis. Prev Chronic Dis. 2018;15:180329. doi: doi: 10.5888/pcd15.180329
17. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(1):31–54. doi: 10.3322/caac.21440
18. Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to Diet and Physical Activity Cancer Prevention Guidelines and Cancer Outcomes: A Systematic Review. Cancer Epidemiol Biomarkers Prev. 2016;25(7):1018–28. doi: 10.1158/1055-9965.EPI-16-0121.

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occurrence of this malignancy and the possibilities of prevention. In recent years, in both sexes, a decrease in deaths caused by colorectal cancer has been noted, which speaks of the improvement of diagnostics and treatment of this malignancy.

Competing interests

The authors declared no competing interests.

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References

1. Cancer today [Internet]. [cited 2023 May 27]. Available from: http://gco.iarc.fr/today/home
2. Colorectal Cancer Awareness Month 2022 – IARC [Internet]. [cited 2023 May 27]. Available from: https://www.iarc.who.int/featured-news/colorectal-cancer-awareness-month-2022/
3. Cancer and obesity [Internet]. [cited 2023 May 27]. Available from: http://gco.iarc.fr/obesity/home
4. IZJZS - Batut: Publikacije [Internet]. [cited 2023 May 27]. Available from: https://www.batut.org.rs/index.php?category_id=9
5. Segi M. Cancer mortality for selected sites in 24 countries (1950-57). Sendai, Japan: Department of Public Health, Tohoku University of Medicine; 1960.
6. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3):335–51. doi: 10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z
7. Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Gastroenterol Rev. 2019;14(2):89–103. doi: doi: 10.5114/pg.2018.81072
8. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683–91. doi: doi: 10.1136/gutjnl-2015-310912.
9. Edwards BK, Ward E, Kohler BA, Eheman C, Zauber AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer. 2010;116(3):544–73. doi: doi: 10.1002/cncr.24760.
10. SEER*Explorer Application [Internet]. [cited 2023 Jun 1]. Available from: https://seer.cancer.gov/statistics-network/explorer/application.html
11. American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.
12. Levin B, Lieberman DA, McFarland B, Smith RA, Brooks D, Andrews KS, et al. Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology*†. CA Cancer J Clin. 2008;58(3):130–60. doi: 10.3322/CA.2007.0018
13. Chatenoud L, Bertuccio P, Bosetti C, Levi F, Curado MP, Malvezzi M, et al. Trends in cancer mortality in Brazil, 1980–2004. Eur J Cancer Prev. 2010;19(2):79.
14. Malvezzi M, Bosetti C, Chatenoud L, Rodríguez T, Levi F, Negri E, et al. Trends in cancer mortality in Mexico, 1970–1999. Ann Oncol. 2004;15(11):1712–8. doi: doi: 10.1093/annonc/mdh424.
15. Scaling up cancer diagnosis and treatment in developing countries: what can we learn from the HIV/AIDS epidemic? Ann Oncol. 2010;21(4):680–2. doi: doi: 10.1093/annonc/mdq055.
16. Yu W, Jiang J, Xie L, Li B, Luo H, Fu Y, et al. Mortality Trends in Colorectal Cancer in China During 2000–2015: A Joinpoint Regression and Age-Period-Cohort Analysis. Prev Chronic Dis. 2018;15:180329. doi: doi: 10.5888/pcd15.180329
17. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(1):31–54. doi: 10.3322/caac.21440
18. Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to Diet and Physical Activity Cancer Prevention Guidelines and Cancer Outcomes: A Systematic Review. Cancer Epidemiol Biomarkers Prev. 2016;25(7):1018–28. doi: 10.1158/1055-9965.EPI-16-0121.

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