



# Epidemiologija malignih tumora i skrining u onkologiji

## Epidemiology of malignant tumors and screening in oncology

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### Apstrakt

Epidemiologija malignih tumora predstavlja proučavanje distribucije i determinanti ovih bolesti, sa ciljem da identificuje uzroke i utvrdi mere prevencije. Epidemiologija malignih tumora je oruđe za procenu rizika, za preporuku odgovarajućeg skrining programa za populacije visokog rizika i procenu uspešnosti sprovedenih mera prevencije.

Svetsku populaciju danas čini više od 6 milijardi ljudi. Prema podacima SZO danas je u svetu više od 30 miliona obolelih od raka (prevalencija), a svake godine oboli oko 18,1 milion ljudi. Broj umrlih od malignih tumora 2018. godine iznosio je 9,6 miliona sa predviđanjima da 2020. god umre 12 miliona. Tokom života, jedan od pet muškaraca, i jedna od šest žena će oboleti od raka, a jedan od osam muškaraca i jedna od jedanaest žena će umreti od nekog oblika maligne bolesti. Trend povećanja broja obolelih je u korelaciji sa ukupnim porastom stanovništva i starenjem populacije, učestalosti faktora rizika i stilom života. Skoro polovina novih slučajeva malignih tumora i više od polovine smrtnih slučajeva od raka u svetu 2018. godine je registrovano u Aziji, s obzirom na to da na ovom kontinentu živi skoro 60% svetske populacije. U Evropi, koja čini samo 9% svetske populacije, registrovano je 23,4% svih slučajeva raka i 20,3% smrtnosti od raka. U Americi koja čini 13,3% svetske populacije, registrovano je 21% novo obolelih i 14,4% umrlih od raka. Veći procenat umrlih od raka u odnosu na procenat novootkrivenih je registrovan u Aziji (57,3% i 48,4%) i u Africi (7,3% i 5,8%).

Rak pluća, rak dojke i rak debelog creva su vodeće lokalizacije u oboljevanju i umiranju u svetu i čine zajedno jednu trećinu novoobolelih i umrlih osoba od raka u svetu. U svetu je najveća učestalost raka pluća, sa trendom pada u razvijenim zemljama, a rasta u zemljama u razvoju. Incidencija raste kod raka dojke, grlića, kolorektalnog karcinoma, prostate, melanoma kože, testisa, a jajnika negde raste, dok negde pada, leukemije i limfomi se ne menjaju. Incidencija grlića materice pada u EU. U svetu pada mortalitet raka dojke, grlića materice, kolorektalnog karcinoma kao rezultat sprovođenja skrining programa, kao i raka testisa, dok se rak prostate ne menja.

U Srbiji je 2015. godine ukupan broj obolelih od malignih tumora bio oko 150.000, broj novoobolelih 36.000, a umrlih više od 20.000. Vodeće lokalizacije u 2015. godini, kod žena su: rak dojke sa 24%, kolorektalni karcinom oko 10%, karcinom pluća oko 10%, rak grlića materice oko 6,3%, rak uterusa 5,7% i rak ovarijuma 4,4%. Muškarci najviše oboljevaju od karcinoma pluća 19,6%, kolorektalnog karcinoma 13,4%, karcinoma prostate 10,2%, karcinoma mokraće bešike 6,6% i karcinoma želuca 3,7%. Srbija se, prema procenama Internacionale agencije za istraživanje raka, među 40 zemalja Evrope, svrstava u grupu zemalja sa srednjim rizikom oboljevanja (nalazi se na 12. mestu) i visokim rizikom od umiranja (2. mesto odmah posle Mađarske) od malignih tumora u Evropi. Procenjene stope obolovanja i umiranja od svih malignih tumora su niže kod muškaraca nego kod žena.

### Abstract

The epidemiology of malignant tumors is the study of the distribution and determinants of these diseases, with the aim of identifying the causes and determining prevention measures. The epidemiology of malignant tumors is a tool for risk assessment, for recommending an appropriate screening program for high-risk populations, and for assessing the success of implemented prevention measures.

Nowadays, the world's population is more than 6 billion people. According to the WHO, today there are more than 30 million cancer patients in the world (prevalence), and about 18.1 million people get sick every year. The number of deaths from malignant tumors in 2018 was 9.6 million, with predictions that 12 million will die in 2020. During their lifetime, one in five men and one in six women will develop cancer, and one in eight men and one in eleven women will die from some form of malignancy. The trend of increasing the number of patients is correlated with the total population growth and population aging, the frequency of risk factors, and lifestyle. Almost half of new cases of malignant tumors and more than half of cancer deaths in the world in 2018 were registered in Asia, considering that almost 60% of the world's population lives on this continent. In Europe, which makes up only 9% of the world's population, 23.4% of all cancer cases and 20.3% of cancer deaths are registered. In America, which makes up 13.3% of the world's population, 21% of new cases and 14.4% of cancer deaths have been registered. A higher percentage of cancer deaths compared to the percentage of newly diagnosed was registered in Asia (57.3% and 48.4%) and in Africa (7.3% and 5.8%).

Lung cancer, breast cancer, and colon cancer are the leading localizations in morbidity and mortality in the world and together constitute one-third of newly diagnosed and died of cancer in the world. The world has the highest incidence of lung cancer, with a declining trend in developed countries and an increase in developing countries. The incidence increases with breast, cervical, colorectal cancer, prostate, melanoma of the skin, testicles, and the ovaries grow somewhere while falling, leukemias and lymphomas do not change. The incidence of the cervix is falling in the EU. The mortality of breast cancer, cervical cancer, colorectal cancer is falling in the world as a result of the implementation of screening programs, as well as testicular cancer, while prostate cancer is not changing.

In Serbia, in 2015, the total number of patients with malignant tumors was around 150,000, the number of newly diagnosed patients was 36,000, and the number of deaths was more than 20,000. Leading localization in 2015, women are breast cancer 24%, colorectal cancer about 10% of lung cancer about 10% of cervical cancer around 6.3%, 5.7% of uterine cancer and ovarian cancer is 4.4%. Men suffer the most from lung cancer 19.6%, colorectal cancer 13.4%, prostate cancer 10.2%, bladder cancer 6.6% and gastric cancer 3.7%. According to the estimates of the International Agency for Research on Cancer, Serbia ranks among the 40 countries in Europe in the group of countries with a medium risk of disease (ranked 12th) and a high risk of dying (2<sup>nd</sup> place immediately after Hungary) from malignant tumors in Europe. Estimated rates of morbidity and mortality from all malignant tumors are lower in men than in women.

Analitičkom epidemiologijom su najčešći identifikovani uzročnici malignih oboljenja: duvan sa oko 25-35% smrtnosti, alkohol sa 3%, dijeta i način ishrane sa 30%, infekcije sa 5%, profesionalno izlaganje agensima sa 5%, ionizujuće zračenje naročito kod dece 2%, nejonizujuće zračenje, medikamenti, genetska sklonost 2%. Na približno dve trećine faktora rizika koji su odgovorni za nastanak malignih tumora moguće je uticati, menjati ih ili ih eliminisati. Čak 40% malignih tumora je moguće izbjeći smanjenjem nezdravih stilova života. Ukoliko do bolesti ipak dode, njen ishod je moguće poboljšati ranim otkrivanjem, adekvatnim lečenjem i rehabilitacijom uz odgovarajuće palijativno zbrinjavanje.

U okviru programa prevencije razlikuju se primarna, sekundarna i tercijska prevencija. Primarna prevencija podrazumeva sprečavanje nastanka bolesti redukcijom ili eliminisanjem izloženosti uzročnim faktorima rizika ili imunizacijom, odnosno označava intervencije pre nastanka bolesti. Sekundarna prevencija podrazumeva skrining, otkrivanje bolesti u ranoj fazi bolesti tj. u presimptomatskoj fazi (interval od nastanka bolesti do pojave kliničkih simptoma i znakova bolesti) i rano lečenje. Tercijska prevencija se odnosi na lečenje bolesnih osoba u kliničkoj fazi bolesti, a u cilju prevencije komplikacija bolesti uključujući smrtni ishod. Posebnu ulogu u ranom otkrivanju malignih tumora imaju skrining programi, kao vid sekundarne prevencije. Značaj skrininga je u dokazano smanjenju smrtnosti za određeno maligno oboljenje. Skrining je program individualnog testiranja populacije korišćenjem različitih postupaka (fizikalni pregled, laboratorijska i dijagnostička procedura, upitnik itd...), gde pojedinac nema nijedan vidljiv simptom bolesti, da bi se otkrile one osobe koje već imaju razvijenu bolest ili veliku šansu da je dobiju. Skrining može biti selektivni, oportunistički, multipli (multifazni), i masovni (organizovani). Organizovani (masovni) skrining predstavlja organizovano masovno pozivanje ciljne populacije na testiranje i tumačenje testova, praćeno kontrolom kvaliteta i izveštavanjem. Izvodi se na celokupnoj populaciji ili na njenom većem delu. Obično se sprovodi u ciklusima od po nekoliko godina.

Prateći preporuke Svetske zdravstvene organizacije i iskustava evropskih zemalja u sprovođenju populacionih skrining programa, u Srbiji su 2009. godine doneti nacionalni programi, a od decembra 2012. godine je započeto sa sprovođenjem organizovanog decentralizovanog skrininga raka grlića materice, raka dojke i kolorektalnog raka. Na skriningu raka grlića materice obuhvaćene su žene uzrasta od 25 godina do 64 godine, koje se pozivaju na preventivni ginekološki pregled i citološki bris grlića materice (Papa test) jednom u tri godine. Na skrining raka dojke pozivaju se žene starosti od 50 do 69 godina. Mammografski pregledi predviđeni su da se za ovaj uzrast žena rade na dve godine, sa dva nezavisna čitača nalaza. Ciljana grupa za testiranje na rak debelog creva obuhvata građane oba pola, starosti od 50 do 74 godina, koji se jednom u dve godine pozivaju na testiranje na skriveno krvarenje u stolici (iFOB test). Ukoliko je pozitivan test, radi se dalje kolonoskopija i biopsija. Prvi ciklus skrininga raka dojke sproveden je u Srbiji tokom 2013/2014. godine, u 19 opština, pregledano je 78.576 žena i otkriveno je 290 karcinoma. U drugom ciklusu (2015/2016. godine), sprovedenom u 35 opština, pregledano je 99.953 žena i otkriveno je 287 karcinoma. U trećem ciklusu (2017/2018. godina) u 35 opština je pregledano 93.506 žena i otkriveno je 346 karcinoma.

U svetu se pored ova tri skrining programa, istražuju mogućnosti za skrininge drugih malignih tumora, ali još ne postoje prihvate-ne preporuke zbog nepostojanja dovoljno dobrog testa i ubedljivih efekata skrininga. Najviše se istražuje za skrininge raka prostate, želuca, malignog melanoma, jajnika i želuca (za populaciju u Japanu). Organizovani skrining je od ogromnog značaja za smanjenje incidence i mortaliteta od malignih tumora, ali je organizovano veoma zahtevan. Neophodno je i dalje raditi na osnaživanju organizovanog skrininga za rak dojke, rak grlića materice i rak debelog creva na područjima gde se realizuje i investi ga na sva područja naše zemlje gde postoje uslovi za njegovo sprovođenje.

Analytical epidemiology is the most commonly identified cause of malignant diseases: tobacco with about 25-35% mortality, alcohol with 3%, diet and diet with 30%, infections with 5%, occupational exposure to agents with 5%, ionizing radiation, especially in children-2%, non-ionizing radiation, medications, genetic predisposition with 2%. Approximately two-thirds of the risk factors responsible for the development of malignant tumors can be affected, altered, or eliminated. As many as 40% of malignant tumors can be avoided by reducing unhealthy lifestyles. If the disease does occur, its outcome can be improved by early detection, adequate treatment, and rehabilitation with appropriate palliative care.

There is primary, secondary, and tertiary prevention within the prevention program. Primary prevention means preventing the onset of the disease by reducing or eliminating exposure to causal risk factors or immunization, ie means interventions before the disease onset. Secondary prevention includes screening, detection of diseases at an early stage of the disease, i.e., in the presymptomatic phase (interval from the onset of the disease to the appearance of clinical symptoms and signs of the disease), and early treatment. Tertiary prevention refers to the treatment of sick persons in the clinical phase of the disease, in order to prevent complications of the disease, including death. Screening programs, as a type of secondary prevention, have a special role in the early detection of malignant tumors. The importance of screening is in the proven reduced mortality for a particular malignant disease. Screening is a program of individual testing of the population using various procedures (physical examination, laboratory and diagnostic procedure, questionnaire, etc.), where an individual does not have any visible symptoms of the disease, to detect those who already have the disease or a high chance of getting it. Screening can be selective, opportunistic, multiple (multiphase), and mass (organized). Organized (mass) screening is an organized mass invitation of the target population for testing and interpretation of tests, followed by quality control and reporting. It is performed on the entire population or on a larger part of it. It is usually carried out in cycles of several years.

Following the recommendations of the World Health Organization and the experiences of European countries in the implementation of population screening programs, national programs were adopted in Serbia in 2009, and in December 2012 the implementation of organized decentralized screening for cervical cancer, breast cancer, and colorectal cancer began. Cervical cancer screening includes women aged 25 to 64, who are invited for a preventive gynecological examination and a cytological smear of the cervix (Pap test) once every three years. Women aged 50 to 69 are invited for breast cancer screening. Mammographic examinations are planned for this age of women for two years, with two independent readers of the findings. The target group for testing for colon cancer includes citizens of both sexes, aged 50 to 74, who are invited once every two years for testing for hidden bleeding in the stool (iFOB test). If the test is positive, colonoscopy and biopsy are performed. The first cycle of breast cancer screening was conducted in Serbia during 2013/2014, in 19 municipalities, 78,576 women were examined and 290 cancers were detected. In the second cycle (2015-2016), conducted in 35 municipalities, 99,953 women were examined and 287 cancers were detected. In the third cycle (2017/2018), 93,506 women were examined in 35 municipalities and 346 cancers were detected.

In addition to these three screening programs, the world is exploring the possibilities for screening other malignant tumors, but there are still no accepted recommendations due to the lack of a test that is good enough to be performed, and convincing screening effects. It is mostly researched for screening for the prostate, stomach, malignant melanoma, ovarian and stomach cancers (for the population in Japan). Organized screening is of great importance for reducing the incidence and mortality from malignant tumors, but the organization is very demanding. It is necessary to continue working on strengthening the organized screening for breast cancer, cervical cancer, and colon cancer in the areas where it is realized and to introduce it in all areas of our country where there are conditions for its implementation.