

## PREVENCIJA ATEROSKLOROZE S OSVRTOM NA GOJAZNOST I NEADEKVATNU ISHRANU KAO FAKTORE RIZIKA ZA NASTANAK KARDIOVASKULARNIH BOLESTI

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### SAŽETAK

U ovom radu biće predstavljene informacije iz relevantnih izvora podataka u vezi sa prevencijom ateroskleroze s osvtom na gojaznost i neadekvatnu ishranu kao faktore rizika za nastanak kardiovaskularnih bolesti (KVB). Svetska zdravstvena organizacija procenjuje da svake godine od KVB umre 17,9 miliona ljudi, što je trećina ukupnog broja umrlih u svetu. KVB su ne samo vodeći uzrok umiranja, nego i obolenja i nesposobnosti, što ukazuje na njihov veliki javnozdravstveni značaj. Smatra se da je endotelna disfunkcija rana faza ateroskleroze. Aterosklerozu se javlja i kod dece mlađe od 10 godina, dok rizik od ateroskleroze raste sa godinama starosti. Postoji preko 300 faktora povezanih sa aterosklerozom i njenim ključnim komplikacijama, koronarnim oboljenjem srca i moždanim udarom. Najvažniji od njih su gojaznost, fizička neaktivnost, hipertenzija, pušenje, neadekvatna ishrana, abnormalne vrednosti lipida, nasleđe, metabolički sindrom, dijabetes i psihosocijalni faktori. Redukcijom ili eliminacijom svih navedenih faktora rizika može se doprineti smanjivanju rizika od KVB. Neophodna su dalja istraživanja u ovoj oblasti sa ciljem boljeg definisanja nezavisnih faktora rizika za nastanak ateroskleroze i posledičnih KVB.

**Ključne reči:** kardiovaskularne bolesti, aterosklerozu, gojaznost, ishrana, faktori rizika, prevencija

### Uvod

Svetska zdravstvena organizacija (SZO) procenjuje da svake godine od kardiovaskularnih bolesti (KVB) umre 17,9 miliona ljudi, što čini oko 32% ukupnog broja umrlih (1). Broj umrlih od KVB je manji u razvijenim zemljama koje imaju program mera prevencije, dok više od ¾ umrlih od KVB je u srednje i slabo razvijenim zemljama (1-4).

KVB su ne samo vodeći uzrok umiranja, nego i obolenja i nesposobnosti, što ukazuje na njihov veliki javnozdravstveni značaj. KVB obuhvataju: ishemijske bolesti srca (IBS), cerebrovaskularne bolesti (CVB) i periferne arterijske bolesti (5). Podaci govore da je od 1950. godine do danas došlo do pada umiranja od KVB u većini razvijenih zemalja sveta.

Framingamska studija je bila prva studija u kojoj je uočena veza između životnih navika i KVB (2). Danas se navodi da postoji preko 300 faktora povezanih sa aterosklerozom i njenim ključnim komplikacijama, IBS i moždanim udarom (6). Na-

jvažniji od njih su gojaznost, fizička neaktivnost, hipertenzija, pušenje, neadekvatna ishrana, abnormalne vrednosti lipida, nasleđe, metabolički sindrom, dijabetes i psihosocijalni faktori (7,8).

U ovom radu biće predstavljene informacije iz relevantnih izvora podataka u vezi sa prevencijom ateroskleroze s osvtom na gojaznost i neadekvatnu ishranu kao faktore rizika za nastanak KVB.

### Aterosklerozu

Aterosklerozu je vodeći uzrok nastanka KVB. To je hronično inflamatorno oboljenje koje karakteriše prisustvo imunokompetentnih ćelija koje proizvode proinflamatorne citokine u lezijama. Takođe, tu su u obilju mrtve ćelije, kao i oksidisani oblici lipoproteina male gustine (LDL holesterol) (7).

Aterosklerozu može da se javi u ranim godinama života (9) i dovodi se u vezu sa brojnim faktorima, a manifestuje se različitim patoanatomskim

## PREVENTION OF ATHEROSCLEROSIS WITH REFERENCE TO OBESITY AND INADEQUATE NUTRITION AS RISK FACTORS FOR CARDIOVASCULAR DISEASES

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### SUMMARY

This paper will present information from relevant data sources regarding the prevention of atherosclerosis, focusing on obesity and inadequate nutrition as risk factors for cardiovascular diseases (CVDs). The World Health Organization estimates that 17.9 million people die from CVDs each year, equaling a third of the world's death toll. CVDs are not only the leading cause of death but also of illness and disability, which indicates their great public health importance. Endothelial dysfunction is thought to be an early stage of atherosclerosis. Atherosclerosis also occurs in children under the age of 10, while the risk of atherosclerosis increases with age. There are over 300 factors associated with atherosclerosis and key complications, coronary heart disease, and stroke. The most important of these are obesity, physical inactivity, hypertension, smoking, inadequate diet, abnormal lipid values, heredity, metabolic syndrome, diabetes, and psychosocial factors. Reducing or eliminating all of these risk factors can help reduce the risk of CVDs. Further research in this area is needed to better define the independent risk factors for atherosclerosis and consequent CVD.

**Keywords:** atherosclerosis, cardiovascular diseases, obesity, diet, risk factors, prevention

### Introduction

The World Health Organization (WHO) estimates that 17.9 million people die each year from cardiovascular diseases (CVDs), accounting for about 32% of all deaths (1). According to the data of the World Health Organization (WHO), every year, 17.9 million people die from cardiovascular diseases (CVDs), representing 32% of all global deaths (1). The number of deaths caused by CVDs is smaller in developed countries, which have prevention measure programs, while more than three-quarters of CVD deaths take place in low and middle-income countries (1-4).

CVDs are not only the leading cause of death but also illness and disability, which indicates their great public health importance. CVDs include coronary heart disease (CHDs), cerebrovascular diseases (CVDs), and peripheral arterial diseases (5). The data show that from 1950 until today, there has been a drop in CVD deaths in most developed countries of the world.

The Framingham study was the first study that observed a link between life habits and CVD (2). Today, it is stated that there are over 300 factors associated with atherosclerosis and its key complications, CHD and stroke (6). The most important of these are obesity, physical inactivity, hypertension, smoking, inadequate nutrition, abnormal lipid values, heredity, metabolic syndrome, diabetes, and psychosocial factors (7,8).

This paper will present information from relevant data sources related to the prevention of atherosclerosis with reference to obesity and inadequate nutrition as risk factors for CVD.

### Atherosclerosis

Atherosclerosis is the main cause of CVD. It is a chronic, inflammatory disease characterized by the presence of immunocompetent cells that produce proinflammatory cytokines in lesions. Also, there

promenama, počevši od masnih pruga do kompleksnih ulcerisanih plakova. Kada se desi erozija, ruptura i nagli rast plaka, dešava se tromboza u krvnom sudu što dovodi na nivou koronarnih krvnih sudova do akutnog koronarnog sindroma.

Za nastanak ateroskleroze najznačajniji faktori rizika su dislipoproteinemija, odnosno poremećaji u metabolizmu lipida (10). U brojnim studijama visoke vrednosti lipoprotein (a) (Lp(a)) u serumu dovode se u vezu sa KVB, tako da predstavlja nezavisan faktor rizika za nastanak KVB (11).

U literaturi se navodi da se aterosklerotske promene mogu javiti i kod dece mlađe od 10 godina (10). Starost je nezavisan faktor rizika za nastanak ateroskleroze. Starenjem, usled loših sredinskih (neadekvatna ishrani, gojaznost, fizička neaktivnost, pušenje, prekomerna upotreba alkohola) i genetskih faktora, aterosklerozu se sve više razvija (10).

## Gojaznost

Gojaznost je hronična bolest koja je veoma rasprostranjena, a prevalencija ove bolesti veoma varira u svetu i kreće se u opsegu 20-45%. Definiše se kao indeks telesne težine koji je jednak ili veći od  $30 \text{ kg/m}^2$  (12). Gojaznost je rezultat prekomernog nakupljanja masti u organizmu i povećanja težine (3). Ona je faktor rizika za širok spektar bolesti, a pogotovo za aterosklerozu i KVB.

Mnoge velike studije kardiometaboličkog rizika potvrdile su da je višak visceralne gojaznosti snažno povezan s metaboličkim abnormalnostima za koje se u početku smatralo da su povezane s viškom debljine same po sebi (13). Merenjem obima struka procenjuje se veličina intraabdominalnog masnog tkiva. Osobe sa obimom struka koji je preko 94 cm (za muškarce) i preko 80 cm (za žene) imaju povećan rizik, a sa obimom struka preko 102 cm (za muškarce) i preko 88 cm (za žene) imaju jako povećan rizik za nastanak komorbiditeta, pre svega KVB.

Gojazne osobe imaju dva puta veću prevalenciju hipertrigliceridemije nego osobe koje nisu gojazne (14). Takođe, kod gojaznih osoba, kao i kod osoba sa prekomernom telesnom težinom, češća je pojava hipertrigliceridemija sa visokim vrednostima LDL holesterola i niskim vrednostima lipoproteina velike gustine (HDL holesterol) (15,16).

Najznačajnije je kod pregleda gojaznog bolesnika uzeti detaljnu anamnezu, kao i uraditi fizički

pregled i laboratorijske analize (17). Fizički pregled podrazumeva merenje težine, visine, obima struka i krvnog pritiska, određivanje indeksa telesne mase i utvrđivanje postojanja komorbiditeta. Takođe je neophodno uraditi elektrokardiogram. Minimum laboratorijskih analiza koje je neophodno uraditi obuhvata fizičko-hemijski pregled urina, glikemiju našte i 2 sata posle jela, aspartat aminotransferazu, alalnin aminotransferazu, gama glutamil transferazu, lipidski status i tiroidni stimulirajući hormone (TSH).

Cilj lečenja gojaznosti je redukcija prekomerne težine, smanjivanje uticaja ili eliminacija drugih faktora rizika i postojećih komorbiditeta. Lekari primarne zdravstvene zaštite, tj. izabrani lekari imaju značajnu ulogu u tome. Lečenje gojaznih osoba bi trebalo da obuhvata odgovarajuću hipokalorijsku ishranu i povećanu fizičku aktivnost, tj. promenu stila života (18,19). Preporuka je da dnevni kalorijski unos treba da bude smanjen za 500-1000 kCal u odnosu na stvarne potrebe. Gubitak telesne mase treba da bude od 5 do 15% od inicijalne težine da bi postojao povoljan efekat na komorbiditete. Kod nekih osoba dobre rezultate može da da jedino primena farmakoterapije ili hirurško lečenje. Za smanjenje telesne mase motivacija osobe je jako važna, te je neophodno pre tretmana utvrditi njenu spremnost i motivisanost i po potrebi uključiti multidisciplinarni tim na čelu sa psihologom (17).

## Ishrana

Ishrana koja je bogata zasićenim mastima značajno doprinosi nastanku IBS usled povećanja LDL-holesterola u serumu. Korekcija ovakve „aterogene“ ishrane i promena stila života su ključni u borbi protiv IBS. Preporuke za pravilnu i uravnoteženu ishranu odnose se na konzumiranje povrća i voća, žitarica od celog zrna, orašastih plodova i dosta vlakana, mršavog mesa, ribe i devičanskog maslinovog ulja što je najsličnije mediteranskoj ishrani (20,21).

U cilju prevencije ateroskleroze, pa samim tim i nastanka KVB, predlaže se niska potrošnja soli i hrane životinjskog porekla, kao i povećan unos biljne hrane – voća, povrća, integralnih žitarica, mahunarki i orašastih plodova – povezanih sa manjim kalorijskim unosom (22). Poseban akcent se stavlja na redukciji unosa maslaca, masti i drugih zasićenih masti, kao i na njihovoj zameni

are a lot of necrotic cells, as well as oxidized forms of low-density lipoproteins (7).

Atherosclerosis can occur in the early years of life (9), and it is associated with a number of factors, while it is manifested in various pathoanatomical changes, ranging from fatty streaks to complex plaque ulcers. When erosion, rupture, and sudden growth of plaque occur, thrombosis occurs in the blood vessel, which leads to acute coronary syndrome at the level of coronary blood vessels.

The most important risk factors for atherosclerosis are dyslipoproteinemia, that is, disorders in lipid metabolism (10). In a number of studies, high levels of serum lipoprotein (a) (Lp (a)) have been linked to CVD, and it is an independent risk factor for CVD (11).

It is stated in the literature that atherosclerotic changes may appear in children younger than 10 years (10). Age is an independent risk factor for atherosclerosis. As we age, due to bad habits (inadequate diet, obesity, physical inactivity, smoking, excessive alcohol use) and genetic factors, atherosclerosis develops more and more (10).

## Obesity

Obesity is a chronic disease that is very widespread, and the prevalence of this disease varies greatly and ranges from between 20-45% in the world. It is defined as the body mass index equal to or higher than  $30 \text{ kg/m}^2$  (12). It is the result of excessive accumulation of fat in the body and weight gain (3). Obesity is a risk factor for a wide range of diseases, especially atherosclerosis and CVD.

Many large studies of cardiometabolic risk have confirmed that an excess of visceral obesity is strongly associated with metabolic abnormalities, which were deemed to be linked to excess body weight at the beginning (13). The size of intra-abdominal adipose tissue is estimated by measuring the waist circumference. People with a waist circumference that is over 94 cm (for men) and over 80 cm (for women) have an increased risk, and people with a waist circumference more than 102 cm (for men) and more than 88 cm (for women) have a very increased risk of developing comorbidly, primarily CVDs.

Obese persons have two times higher prevalence of hypertriglyceridemia in comparison to persons who are not obese (14). Also, in obese persons,

as in overweight persons, hypertriglyceridemia with high levels of low-density lipoproteins (LDL cholesterol) and low levels of high-density lipoproteins (HDL cholesterol) is more frequent (15,16).

When examining obese patients, it is most important to take detailed anamnesis, as well as to do a physical examination and laboratory analyses (17). Physical examination involves measuring weight, height, waist circumference, and blood pressure, calculating body mass index, and determining the existence of comorbidities. It is also necessary to do an electrocardiogram. The minimum laboratory tests that need to be done include physical and chemical examination of urine, glycemia on an empty stomach, and two hours after eating, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, lipid status, and thyroid-stimulating hormone.

The goal of treating obesity is to reduce body weight, reduce the impact or eliminate other risk factors and existing comorbidities. Physicians from primary health care, that is, family doctors, have a significant role in that. The treatment of obese persons should include an appropriate low-calorie diet and increased physical activity, that is, the change of lifestyle (18,19). It is recommended that the daily caloric intake should be 500-1000 kCal lesser than the actual need. Weight loss should be 5 to 15% of the initial body weight to give a beneficial effect on comorbidities. In some persons, only pharmacotherapy or surgical treatment can give good results. The person's motivation is very important for reducing body mass, so it is necessary to determine their readiness and motivation before the treatment and, if necessary, involve a multidisciplinary team with a psychologist as a team leader (17).

## Diet

A diet rich in saturated fats significantly contributes to the development of IHD due to an increase in serum LDL-cholesterol. The correction of such "atherogenic" diet and lifestyle changes are key in the fight against IHD. The recommendations for a proper and balanced diet refer to the consumption of vegetables and fruits, whole grains, nuts and a lot of fiber, lean meat, fish, and virgin olive oil, which is most similar to

nezasićenim mastima (posebno maslinovim uljem). Većem riziku od KVB doprinosi konzumiranje crvenog mesa i mesnih prerađevina, a manje konzumacija ribe. Namirnice sa visokim glikemijskim indeksom treba zameniti namirnicama sa niskim glikemijskim indeksom kao što su žitarice od celog zrna. Manji rizik od KVB imaju osobe koje konzumiraju niske količine alkohola, kafe i čaja, a veći oni koji unose bezalkoholna pića zbog sadržaja šećera u njima.

Nekonzistentni rezultati postoje po pitanju značaja uzimanja beta-karotena ili drugih antioksidanasa u cilju redukcije rizika od IBS, što zahteva dalja istraživanja u ovoj oblasti (23). Studija Yang i saradnika, ukazuje da namirnice koje su bogate antioksidansima poput ishrane koja se koristi u Kineskoj alternativnoj medicini ima jedinstvene prednosti u prevenciji IBS (24).

Nizak kalorijski unos može povećati rizik od nedovoljnog unosa polinezasićenih masnih kiselina (engl. *polyunsaturated fatty acids* – PUFA), može narušiti apsorpciju vitamina rastvorljivih u masti i biti povezan sa insuficijencijom drugih esencijalnih hranjivih sastojaka (25). Hrana bogata zasićenim mastima i holesterolom, dovodi do povećanog sistolnog pritiska, hiperglikemije i hiperholesterolemije, nezavisno od drugih faktora rizika (gojaznosti, starosti ili korišćenja alkohola i nikotina) (26). Upotreba mononezasićenih kiselina (u uljima, kao što je maslinovo i suncokretovo), kao i polinezasićenih, doprinosi redukciji vrednosti kako ukupnog holesterola tako i LDL holesterola (25). Veća potrošnja maslinovog ulja dovodi se u vezu sa nižim umiranjem od KVB u mediteranskim zemljama (26).

Studije koje ispituju faktore rizika za nastanak KVB kod dece ukazuju da je sa prevencijom KVB neophodno započeti još u dečijem dobu. Istraživanja ukazuju da je prevalencija hipertenzije kod Turske dece/adolescenata veća nego kod dece/adolesenata srednjeevropskog porekla ali samo kada su pitanju deca/adolescent koji su gojazni ili sa prekomernom telesnom težinom (25). Visok mortalitet i morbiditet od KVB kod dece, ukazuju na potrebu preduzimanja preventivnih mera već u ranom detinjstvu, uz paralelno sprovođenje populacione strategije i strategije visokog rizika (25). Mediteranska ishrana je najpoželjnija za prevenciju KVB i predstavlja idealni nutritivni model za dobro zdravlje (26).

U terapiji gojaznosti prvo mesto zauzima dijetetski režim i fizička aktivnost, ukoliko nema rezultata pristupa se medikamentoznoj terapiji sa orlistatom ili bariatrična hirurgija kada je indeks telesne mase veći od  $40 \text{ kg/m}^2$  (27-29).

## Zaključak

Ateroskleroza dovodi do razvoja KVB, što doprinosi pogoršanju kvaliteta života ljudi i većem riziku od smrti. U cilju prevencije ateroskleroze, a samim tim i KVB, neophodno je edukovati stanovništvo o štetnim faktorima rizika i raditi na njihovoj redukciji i eliminaciji. Poseban akcenat stavlja se na značaj fizičke aktivnosti, smanjenja telesne težine i adekvatnoj ishrani. Mediteranska dijeta se navodi kao ključna u prevenciji KVB.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

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the Mediterranean diet (20,21).

In order to prevent atherosclerosis, and thus the development of CVD, low consumption of salt and food of animal origin is proposed, as well as increased intake of plant foods - fruits, vegetables, whole grains, legumes, and nuts - associated with lower calorie intake (22). Special emphasis is placed on reducing the intake of butter, fats, and other saturated fats, as well as on their replacement with unsaturated fats (especially olive oil). Consumption of red meat and meat products contributes to a higher risk of CVD, while fish consumption contributes to a lower risk. Foods with a high glycemic index should be replaced by foods with a low glycemic index, such as whole grains. People who consume low amounts of alcohol, coffee, and tea have a lower risk of CVDs, and those who consume non-alcoholic drinks are at an increased risk due to their sugar content.

Inconsistent results exist regarding the importance of taking beta-carotene or other antioxidants in order to reduce the risk of IHDs, which requires further research in this area (23). A study by Yang and associated indicates that foods rich in antioxidants, such as the diet used in Chinese traditional medicine, have unique benefits in preventing IHD (24).

Low-calorie intake may increase the risk of insufficient intake of polyunsaturated fatty acids (PUFA), may impair the absorption of fat-soluble vitamins, and may be related to the insufficiency of other nutritive elements (25).

Foods rich in saturated fats and cholesterol lead to increased systolic blood pressure, hyperglycemia, and hypercholesterolemia, independently of other risk factors (obesity, age, or alcohol and nicotine use) (26). The use of monounsaturated acids (in oils such as olive and sunflower), as well as polyunsaturated, contributes to the reduction of both total cholesterol and LDL cholesterol (25). Higher consumption of olive oil is associated with lower deaths from CVD in Mediterranean countries (26).

Studies examining the risk factors for CVDs in children indicate that it is necessary to start preventing CVDs in childhood. Research indicates that the prevalence of hypertension in children/adolescents in Turkey is higher than in children/adolescents of Central European descent, but only in children/adolescents who are obese or overweight (25). High mortality and morbidity

from CVD in children indicate the need to take preventive measures in early childhood, with the parallel implementation of population strategy and high-risk strategy (25). The Mediterranean diet is the most desirable for the prevention of CVD and is an ideal nutritional model for good health (26).

In the treatment of obesity, the dietary regimes and physical activity take the first place, if there are no results, drug therapy with orlistat or bariatric surgery is approached when the body mass index is higher than  $40 \text{ kg/m}^2$  (27-29).

## Conclusion

Atherosclerosis leads to the development of CVD, which contributes to the deterioration of people's quality of life and a higher risk of death. In order to prevent atherosclerosis, and thus CVD, it is necessary to educate the population about harmful risk factors and work on their reduction and elimination. Special emphasis is placed on the importance of physical activity, weight reduction, and adequate nutrition. The Mediterranean diet is cited as key in the prevention of CVDs

## Competing interests

The authors declare no competing interests.

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