doi:10.5937/opmed1904058M

Opšta medicina 2019;25(3-4):58-69

UDC:616-008.6:616.12-056.24

Učestalost i značaj metaboličkog sindroma i njegovih komponenata u ambulantnih pacijenata

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Frequency and importance of metabolic syndrome and its components in outpatients

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Sažetak

Uvod. Metabolički sindrom (MS) predstavlja grupu kardiovaskularnih faktora rizika koji uključuje hiperglikemiju, povišen krvni pritisak, povišene nivoe triglicerida, centralnu gojaznost i sniženi HDL holesterol. Rezultati populacionih studija pokazuju da je MS koristan u prognozi kardiovaskularnog morbiditeta i mortaliteta.

Cilj rada. Ispitati učestalost i značaj metaboličkog sindroma i njegovih pojedinačnih komponenata u ambulantnih pacijenata.

Metod. Studija je obuhvatila 178 (71,26±8,93) ambulantnih pacijenata odabranih metodom slučajnog uzorka, 67 (71,24±9,5) muškaraca i 111 (71,28±11,29) žena (p>0,05). Stanje uhranjenosti je ocenjeno na osnovu antropometrijskih parametara (telesna visina, telesna težina, obim struka). Kod svih ispitanika određivani su glikemija, HDL holesterol, trigliceridi i izmerene su vrednosti krvnog pritiska. Za postavljanje dijagnoze MS korišćeni su kriterijumi Američkog udruženja za srce (*American Heart Association - AHA*) i Nacionalnog instituta za srce, pluća i krv (*National Heart, Lung and Blood Institute - NHLBI*).

Rezultati. Metabolički sindrom je dijagnostikovan kod 42,7% pacijenata, 31,6% muškaraca i 68,4% žena. Učestalost MS je bila veća kod žena (47,7%) u odnosu na muškarce (35,8%) (*p*>0,05); tri komponente MS imalo je 51,3%, četiri 42,1% i pet 6,6% ispitanika. Od pojedinačnih komponenata MS, najčešće je zastupljen povećan obim struka (92,1%). Sa koronarnom bolešću bilo je ukupno 10,5% pacijenata sa MS, a u grupi pacijenata bez MS 1,96% (*p*<0,01). U posmatranom periodu umrlo je 10,5% pacijenata sa MS i 0,98% bez MS (*p*<0,01).

Zaključak. Učestalost metaboličkog sindroma u populaciji ambulantnih pacijenata je 42,7%, muškaraca 35,8% i žena 46,8%. Povećan obim struka je najčešća pojedinačna komponenta metaboličkog sindroma. Pacijenti sa metaboličkim sindromom imaju značajno veću učestalost koronarne

Abstract

Introduction: Metabolic syndrome (MS) is a group of cardiovascular risk factors including hyperglycemia, elevated blood pressure, elevated triglycerides levels, central obesity, and low HDL cholesterol. Population studies results show MS to be useful in predicting cardiovascular morbidity and mortality.

Objective: Examine the frequency and importance of metabolic syndrome and its components in outpatients.

Methods: The study included 178 (71.26±8.93) outpatients, selected by random sample, 67 (71.24±9.5) men and 111 (71.28±11.29) women (p>0.05). Nutrition status was estimated based on anthropometric parameters (body height, body weight, waist circumference). Glycemia, HDL cholesterol, triglycerides, and blood pressure values were measured in all participants. The criteria of the American Heart Association (AHA/NHLBI) were used to diagnose MS.

Results: MS was diagnosed in 42.7% of the patients, 31.6% of men and 68.4% of women. The incidence of MS was higher in women (47.7%) than men (35.8%) (p>0.05). In subjects with MS, three components were found in 51.3%, four components in 42.1% and five in 6.6%. Considering individual MS components, the increased waist circumference had the highest incidence of 92.1%. Among the patients with coronary heart disease (CHD), 10.2% had MS, and among those without MS only 1.96% (p<0.01). During the observation period, 10.5% of patients with MS died, compared to the group without MS, where 0.98% died (p<0.01).

Conclusion: The incidence of the metabolic syndrome among the outpatients in our group was 42.7%, of whom 35.8% were men and 46.8% were women. Increased waist circumference was the most frequent individual MS component among the participants. Patients with metabolic syndrome have got a significantly higher incidence of coronary artery disease and mortality rates, compared to those without MS, which indicates MS is an important risk factor for the oc-

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bolesti i veći mortalitet nego pacijentini bez MS, što ukazuje da je MS značajan faktor rizika za nastanak i razvoj koronarne bolesti i lošiju prognozu ovih pacijenata, zbog čega moraju biti na odgovarajući način podvrgnut kontroli radi efikasne primarne i sekundarne prevencije.

Ključne reči: metabolički sindrom, učestalost, koronarna bolest, mortalitet.

Uvod

Metabolički sindrom (MS) predstavlja grupu međusobno povezanih fizioloških, biohemijskih, kliničkih i metaboličkih poremećaja, koji direktno i zajedničkim dejstvom povećavaju kardiovaskularni rizik i uključuje hiperglikemiju, povišen krvni pritisak, povišene nivoe triglicerida, abdominalnu gojaznost i sniženi *HDL* holesterol[1,2].

Gojaznost i rezistencija na insulin sa hiperinsulinemijom jesu centralni patofiziološki procesi povezani sa metaboličkim sindromom[3]. Višak insulina može da poveća zadržavanje natrijuma u bubrežnim tubulima i aktivnost simpatičkog nervnog sistema, što dovodi do pojave hipertenzije. Hiperinsulinemija povećava produkciju *VLDL* (*Very low density lipoproteine*) u jetri sa posledičnim smanjenjem koncentracije *HDL* holesterola[4].

Disfunkcionalna proizvodnja adipokina, posebno u hipertrofičnom masnom tkivu, predstavlja patogenetsku vezu između centralne akumulacije masti, rezistencije na insulin, hiperlipidemije i hipertenzije i prethodi razvoju metaboličkih i vaskularnih poremećaja[5].

Učestalost MS u svetu kreće se u rasponu <10% do 84% u zavisnosti od područja - seoske ili gradske sredine, sastava populacije, kao i definicije metaboličkog sindroma[2]. Međunarodno udruženje za dijabetes (*IDF*) procenjuje da 25% svetske odrasle populacije ima MS i da od komplikacija ovog sindroma godišnje u svetu umire 3,2 miliona ljudi[2,6]. Viši socioekonomski status, sedentaran način života i visok indeks telesne mase (*BMI*), značajno su povezani sa MS[2]. Učestalost MS je 5% među ispitanicima normalne težine (*BMI* <25,0 *kg*/*m*²), 22% sa prekomernom težinom0 (*BMI* 25-29,9 *kg*/*m*²) i 60% kod gojaznih (*BMI* >30,0 *kg*/*m*²)[2].

Rezultati populacionih studija pokazuju da je MS koristan u predikciji kardiovaskularnog morbiditeta i mortaliteta i smatra se glavnim uzročnikom epidemije kardiovaskularnih bolesti[5].

Pacijenti sa MS imaju dvostruko veći rizik za nastanak kardiovaskularnih bolesti, petostruko za nastanak dijabetesa i dva do četiri puta veći rizik za nastanak moždanog udara[7,8]. Ova lica imaju tri do četiri puta veću verovatnoću za nastanak infarkta miokarda i dva puta veći rizik smrti od infarkta[5,7,8].

Zbog različitih kriterijuma za definisanje MS, epidemi-

curence and development of the coronary heart disease. The patients with MS have got a worse medical prognosis and that's why they should have regular check- ups, for the sake of primary and secondary prevention.

Keywords: metabolic syndrome, frequency, coronary heart disease, mortality.

Introduction

Metabolic syndrome (MS) comprises the group of interrelated physiological, biochemical, clinical and metabolic disorders which directly and synergically increase cardiovascular risk. MS includes hyperglycemia, elevated blood pressure, elevated triglyceride levels, abdominal obesity, and decreased HDL cholesterol levels.[1,2]

Obesity and insulin resistance, with hyperinsulinemia, are central pathophysiologic mechanisms connected with metabolic syndrome.[3] Insulin excess can increase sodium retention in the renal tubules and the activity of the sympathetic nervous system, which consequently leads to hypertension.

Hyperinsulinemia increases the production of VLDL (*Very low-density lipoprotein*) in the liver, with a consequent decrease in HDL cholesterol levels.[4]

Dysfunctional production of adipokines, especially in the hypertrophic adipose tissue, represents a pathogenic connection between the central accumulation of the fats, insulin resistance, hyperlipidemia, and hypertension, and it precedes the development of metabolic and vascular disorders.[5]

The frequency of MS around the world ranges from <10%, to 84%, depending on the area, urban or rural, population composition, as well as the definition of the metabolic syndrome.[2] International Diabetes Federation (IDF), estimates that 25% of the adults, worldwide, have MS and due to MS complications 3.2 million people die every year.[2,6] Higher socioeconomic status, sedentary lifestyle and high body mass index (BMI) have got a significant connection with MS.[2] The incidence of MS is 5% among the participants with normal weight (BMI<25.0 kg/m^2), 22% in the overweight (BMI 25-29.9 kg/m^2), and 30% in the obese (BMI>30.0 kg/m^2).[2]

Results of the population studies show MS is useful in predicting cardiovascular morbidity and mortality and it`s referred to as the main cause of the epidemics of cardiovascular diseases.[5]

People with MS have got double the risk for cardiovascular diseases, five times higher risk for diabetes, and 2-4 times higher risk for stroke.[7,8] These people have also got 3-4 times higher probability for myocardial infarction and two folds higher risk to die of myocardial infarction.[5,7,8]

Due to the different criteria for defining MS, epidemio-

ološki podaci o učestalosti MS se razlikuju i nisu u potpunosti precizni i uporedivi za različite geografske oblasti i populacije[5].

Cilj rada

Cilj rada je bio da se ispita učestalost i značaj metaboličkog sindroma i njegovih pojedinačnih komponenti u ambulantnih pacijenata.

Metod

Studija je obuhvatila 178 (71,26±8,93 godine) ambulantnih pacijenata, seoske populacije, odabranih metodom slučajnog uzorka, 67 (71,24±9,5 godina) muškaraca i 111 (71,28±11,29 godina) žena (p>0,05).

Primenjeno je opservaciono istraživanje - Studija preseka sprovedena u periodu 2016-2019. god. Svi ispitanici su podvrgnuti kliničkom pregledu i antropometrijskim merenjima, izmeren im je krvni pritisak i uzeta krv za biohemijske analize. Stanje uhranjenosti je ocenjeno na osnovu antropometrijskih parametara (telesna visina, telesna težina, obim struka, obim kukova). Stepen uhranjenosti procenjen je na osnovu vrednosti indeksa telesne mase (*Body Mass Index–BMI*, *kg*/*m*²) koji je dobijen kao količnik vrednosti telesne težine (*kg*) i kvadrata telesne visine izražene u metrima (*m*²).

Obim struka meren je neelastičnom trakom za merenje *BMI* – kalkulator, Hemofarm, u stojećem položaju ispitanika, na sredini između rebarnog luka i grebena ilijačne kosti, na srednjoj aksilarnoj liniji, u nivou umbilikusa, pri ekspirijumu. Uzimanje venske krvi vršeno je u jutarnjim časovima posle prethodnog gladovanja u trajanju od 12 sati. Ukupni holesterol i trigliceridi određivani su metodom oksidaza/peroksidaza, *LDL* i *HDL* holesterol *Direkt* metodom, glikemija metodom glukoza oksidaza/peroksidaza. Sve analize su urađene na aparatu *Biohemijski analizator A15 BioSystems*, korišćenjem reagenasa *BioSystems*. Merenje krvnog pritiska je obavljeno u prepodnevnim časovima, posle kratkog odmora, sfigmomanometrom u sedećem položaju ispitanika.

Za postavljanje dijagnoze metaboličkog sindroma korišćeni su kriterijumi Američkog udruženja za srce (*American Heart Association - AHA)* i Nacionalnog instututa za srce, pluća i krv (*National Heart, Lung and Blood Institute - NHLBI*). Metabolički sindrom su imali pacijenti koji su ispunjavali najmanje tri od sledećih pet kriterijuma: hipertrigliceridemija (*Tgl*>1,7 *mmol*/*l*) ili specifičan tretman za ovu abnormalnost lipida, nizak *HDL* holesterol (<1,03 *mmol*/*l* kod muškaraca i <1,29 *mmol*/*l* kod žena) ili specifičan tretman za ovu abnormalnost lipida; sistolni krvni pritisak >130 *mmHg* i/ili dijastolni krvni pritisak >85 *mmol*/*L* ili antihipertenzivna terapija; glikemija natašte >5,6 *mmol*/*L* ili antidijabetička terapija i obim struka >102 *cm* kod muškaraca i >88 *cm* kod žena[9].

logical data on the incidence of MS defer and are not quite precise and comparable for different geographic areas and populations.[5]

Objective

The objective was to evaluate the incidence and the importance of the metabolic syndrome and its singular components in the outpatients.

Methods

The study included 178 outpatients (71.26±8.93 years of age), living in rural areas, selected by random sample, 67 men (71.24±9.5 years of age) and 111 women (71.28±11.29 years of age) (p>0,05).

Observational research was applied – a cross-sectional study conducted from 2016-2019. All the participants underwent a physical examination and anthropometric measuring, their blood pressure was measured and blood was drawn for lab analysis. Nutritional status was appraised according to their anthropometric measures (height, weight, waist circumference, hips circumference). The nutritional level was appraised based on the body mass index (BMI-body weight (kg) divided by body height (meters squared)).

Waist circumference was measured by nonelastic measuring tape (BMI calculator, Hemofarm), with the patient in a standing position, the median between the costal arch and crista iliaca, in the median axillary line, umbilical level, during exhale. Blood was drawn in the morning hours, after 12 hours of fasting. Total cholesterol and triglycerides were measured using oxidase/peroxidase method, LDL and HDL using *Direkt* method, glycemia using glucose oxidase/peroxidase method. All the lab analyses were done using *Biochemical analyzer A15 BioSystems.* Blood pressure measuring was performed in the morning hours, after short patient`s rest, using sphygmomanometer, while the patient was sitting.

American Heart Association (AHA) and National Heart Lung and Blood Institute (NHLBI) diagnostic criteria were used for diagnosing metabolic syndrome. Patients diagnosed with MS had to have at least three out of five diagnostic criteria: hypertriglyceridemia (tgl>1.7 mmol/l) or specific treatment for this lipid abnormality, low HDL cholesterol levels (<1.03 mmol/l in men and <1.29 mmol/l in women) or specific treatment for this lipid abnormality, systolic blood pressure >130 mmHg and/or diastolic blood pressure >85 mmHg or antihypertensive therapy, fasting glucose level > 5.6 mmol/l or antidiabetic therapy, and waist circumference > 102 cm for men and > 88 cm for women.[9]

Data were processed using statistical package SPSS, version 23. Descriptive and analytical methods were used

Podaci su obrađeni upotrebom statističkog paketa *SPSS* verzija 23. U statističkoj analizi podataka korišćeni su deskriptivni i analitički metodi. Od deskriptivnih metoda korišćeni su: srednja vrednost (SV) i standardna devijacija (SD), a od analitičkih statističkih metoda Studentov *t*-test i χ^2-test. Dobijeni rezulati prikazani su tabelarno i grafički.

in statistical data analysis. Used descriptive methods were a median value (MV) and standard deviation (SD) and analytical methods Student`s T-test and X^2 test. Attained results are shown in tables and figures.

Rezultati

Osnovne karakteristike i vrednosti pojedinačnih komponenti MS ispitivanih ambulantnih pacijenata, prikazani su na Tabeli 1.

Results

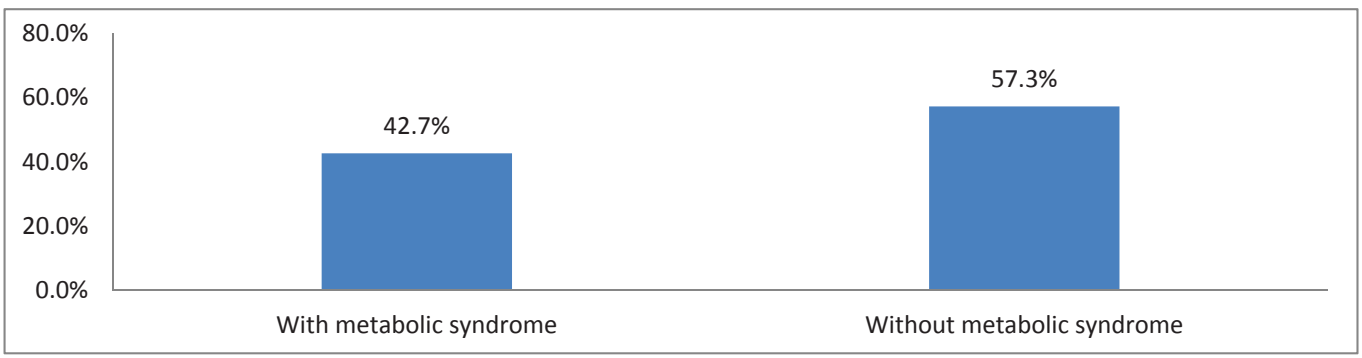
Basic characteristics and values of the singular MS components of the examined outpatients` population are shown in Table 1.

Table 1. Basic characteristics and values of the singular MS components of the examined outpatients` population
Tabela 1. Osnovne karakteristike i vrednosti pojedinačnih komponenata metaboličkog sindroma ispitivane populacije

Parameters	Men (N=67)		Women (N=111)		*P*	Total (N=178)	
	X	SD	X	SD		X	SD
Age	71.2	9.5	71.3	11.3	>0.05	71.2	8.9
BMI (kg/m²)	28.4	5.3	29.8	5.7	>0.05	29.3	5.5
Waist circumference (cm)	97.9	10.9	101.9	12.9	>0.05	100.4	11.7
Glycemia (mmol/L)	9.8	2.2	6.2	2.1	<0.01	6.4	2.1
Total cholesterol (mmol/L)	6.1	1.4	6.5	1.2	<0.05	6.3	1.3
Triglycerides (mmol/L)	1.8	0.9	1.7	0.7	>0.05	1.7	0.8
HDL cholesterol (mmol/L)	1.6	0.7	1.7	0.6	>0.05	1.6	0.6
LDL cholesterol (mmol/L)	3.2	1.0	3.6	0.9	>0.05	3.4	0.9
Blood pressure Systolic (mmHg)	141.9	19.9	142.7	23.6	>0.05	142.0	22.2
Diastolic (mmHg)	85.8	7.3	86.5	8.5	>0.05	86.2	8.1

Metabolički sindrom je bio prisutan kod 76 (42,7%) pacijenata, 024 (31,6%) muškarca i 52 (68,4%) žene; bez MS bila su 102 (57,3%) pacijenta, 43 (42,2%) muškarca i 59 (57,8%) žena. Nije bilo značajne razlike u zastupljenosti između muškaraca i žena sa/bez MS (r>0,05), (Grafikon 1, Tabela 2).

Metabolic syndrome prevailed in 76 (42.7%) patients, 24 (31.6%) men and 52 (68.4%) women; 102 (57.3%) patients were without MS, of whom 43 (42.2%) were men and 59 (57.8%) women. There wasn`t any significant difference in the incidence between men and women with/without MS (p>0.05), (Graph 1, Table 2).



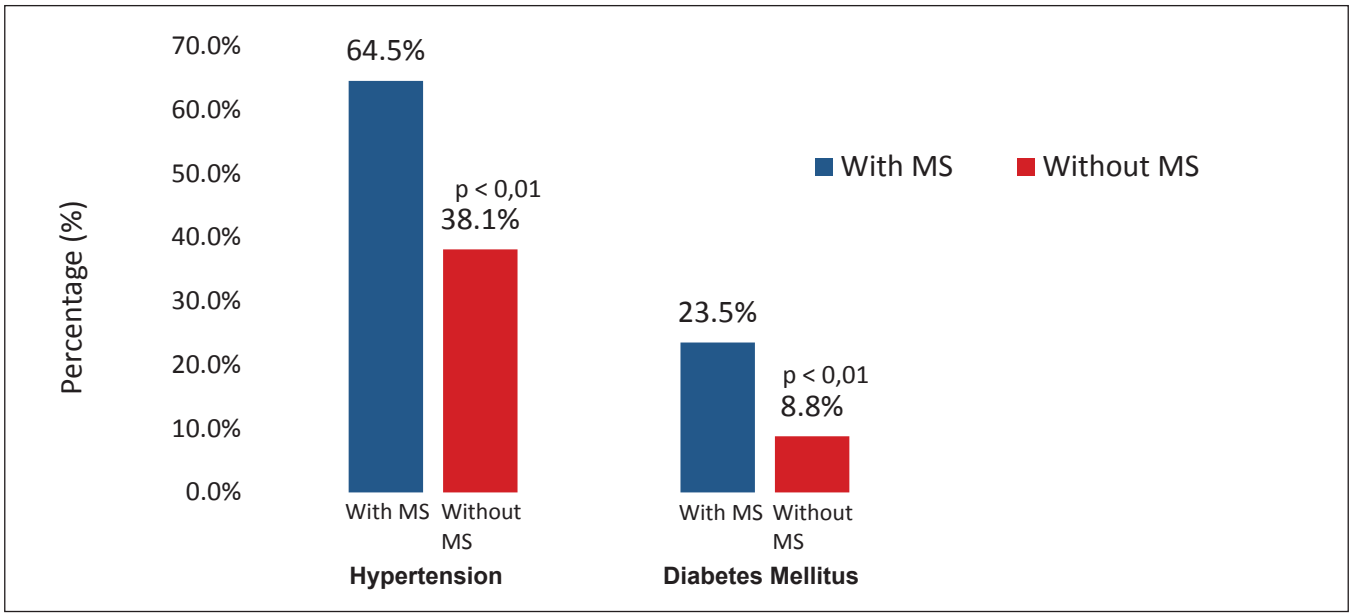
Graph 1. Incidence of metabolic syndrome in the outpatients
Grafikon 1. Učestalost metaboličkog sindroma u ambulantnih pacijenata

Table 2. Values of singular components of metabolic syndrome in patients with or without metabolic syndrome
Tabela 2. Vrednosti pojedinačnih komponenata metaboličkog sindroma u pacijenata sa/bez metaboličkog sindroma

Singular components	**Patients with metabolic syndrome (N=76)**		**Patients without metabolic syndrome (N=102)**		P
	X	**SD**	**X**	**SD**	
Waist circumference (cm)	106.0	11.8	95.7	9.2	<0.01
Triglycerides (mmol/L)	2.1	0.8	1.4	0.5	<0.01
HDL cholesterol (mmol/L)	1.5	0.6	1.7	0.6	<0.05
Glycemia (mmol/L)	7.4	2.7	5.6	1.1	<0.01
Blood pressure					
Systolic (mmHg)	153.0	22.4	134.3	18.4	<0.01
Diastolic (mmHg)	89.7	8.1	83.8	6.9	<0.01
Other parameters					
Age	71.2	10.6	71.3	10.7	>0.05
BMI (kg/m²)	32.3	5.5	27.0	4.3	<0.01
Hip circumference	106.0	10.6	96.9	9.2	<0.01
Total cholesterol (mmol/L)	6.4	1.4	6.3	1.2	>0.05
LDL cholesterol (mmol/L)	3.6	0.9	3.9	0.9	<0.05
Arterial hypertension	49 (64.5%)		24 (23.5%)		<0.01
Diabetes mellitus	29 (38.1%)		9 (8.8%)		<0.01

Ispitanici sa MS imali su značajno veću učestalost hipertenzije (p<0,01) i dijabetesa (p<0,01) u odnosu na one bez MS (Tabela 2, Grafikon 2).

Participants with MS had a significantly higher incidence of hypertension (p<0.01) and diabetes (p<0.01). compared to those without MS (Table 2, Graph 2).



Graph 2. Incidence of hypertension and diabetes mellitus in patients with or without metabolic syndrome
Grafikon 2. Učestlost hipertenzije i dijabetes melitusa u pacijenata sa i bez metaboličkog sindroma

Prosečna starost ispitanika sa MS je 71,2±10,6 godina, bez MS 71,3±10,7 godina, (p>0,05). Učestalost MS bila je veća kod žena (47,7%) nego kod muškaraca (35,8%), ali

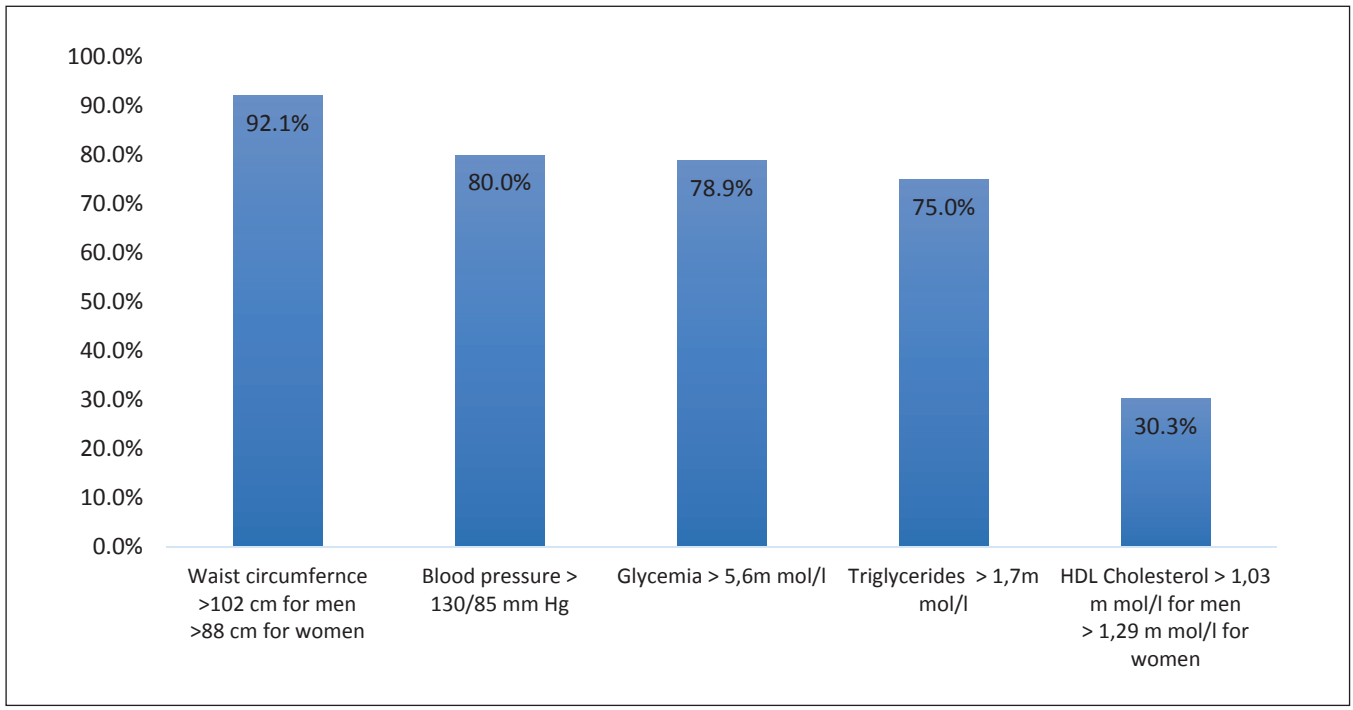
bez statističke značajnosti (*p*>0,05). Kod osoba sa MS tri komponente MS imalo je 39 (51,3%), četiri 32 (42,1%) i pet komponenata 5 (6,6%) ispitanika.

Od pojedinačnih komponenata MS najčešće je zastupljen povećan obim struka - 92,1% (Tabela 3, Grafikon 3).

The average age of the participants with MS was 71.2±10.6 years, and without MS 71.3±10.7 years, (p>0.05). The incidence of MS was higher in women (47.7%), compared to men (35.8%), but without statistical significance (p>0.05). In patients with MS, there were 39 (51.3%) with three components, 32 (42.1%) with four and 5 (6.6%) participants with all five components. The most frequent singular component of MS was waist circumference 92.1% (Table 3, Graph 3).

Table 3. Incidence of singular components of MS in outpatients with MS
Tabela 3. Učestalost pojedinačnih komponenata kod osoba sa MS

Components	**Patients with metabolic syndrome (N=76)**	
	Number	**%**
Waist circumference (cm)	70	92.1
Blood pressure (>130/85 mmHg)	61	80.0
Glycemia (>5/6 mmol/L)	60	78.9
Triglierydes (>1.7 mmol/L)	57	75.0
HDL cholesterol (<1.03 mmol/L for men and <1.29 mmol/L for women)	23	30.3



Graph 3. Incidence of singular components of MS in outpatients with MS
Grafikon 3. Učestalost pojedinačnih komponenata MS kod osoba sa MS

U odnosu na ukupan broj osoba sa/bez MS, sa tri komponente bilo je 21,9%, sa četiri 18,0% i sa pet 2,8% ispitanika. U posmatranom periodu infarkt miokarda imalo je 6 (7,9%) pacijenata sa MS i 2 (1,96%) pacijenta bez MS (p<0,05). Ukupno je, u posmatranom periodu kod svih ispitanika, sa/bez MS bilo 8 (4,49%) sa infarktom miokarda.

Klinički i angiografski dijagnostikovana je angina pektoris kod 2 (2,6%) pacijenta sa MS i nijedna kod pacijenata bez MS. Sa koronarnom bolešću (infarkt miokarda i angina pektoris) bilo je ukupno 8 (10,5%) pacijenata sa MS, a u pacijenata bez MS 2 (1,96%,) (*p*<0,01), (Tabela 4).

Out of all participants (with or without MS), there were 21.9% with 3 components, 18.0% with 4 components, and 2.8% with 5 components. During the observational period, 6 (7.9%) patients with MS had myocardial infarction and 2 (1.96%) patients, without MS (p<0.05). There were a total of 8 (4.49%) participants, with or without MS, during the observational period, who had myocardial infarction. Angina pectoris, diagnosed clinically and angiographically, was found in 2 (2.6%) patients with MS and none without MS.

There was a total of 8 (10.5%) patients with MS who had coronary artery disease (CAD) (myocardial infarction and angina pectoris) and 2 (1.96%,) patients without MS (p<0.01), (Table 4).

Table 4. Incidence of coronary artery disease and mortality in patients with or without MS
Tabela 4. Učestalost koronarne bolesti i mortaliteta u pacijenata sa i bez MS

CAD Mortality	**Outpatients with metabolic syndrome (N=76)**		**Outpatients without metabolic syndrome (N=102)**		P
	N	**%**	**N**	**%**	
CAD	8	10.5	2	1.96	<0.01
Mortality	8	10.5	1	0.98	<0.01

Ukupna učestalost koronarne bolesti u svih pacijenata, sa/bez MS, je 10 (5,6%).

U posmatranom trogodišnjem periodu umrlo je 8 (10,5%) pacijenata sa MS i samo 1 (0,98%) bez MS (p<0,01), (Tabela 4). Ukupno je umrlo 9 (5,05%) pacijenata sa/bez MS.

A total number of patients with CAD, with or without MS, was 10 (5.6%).

In the three year observational period 8 (10.5%) patients with MS died and only 1 (0.98%) patient without MS (p<0.01), (Table 4). Total of 9 (5.05%) patients, with or without patients died.

Diskusija

Ovo istraživanje sprovedeno na relativno malom uzorku starije seoske populacije, pokazalo je visoku učestalost MS (42,7%) među ambulantnim pacijentima. Učestalost MS naših ispitanika u okviru je raširenosti MS kod starijih osoba (22,3%-67,9%)[10], slična je evropskim zemljama - Holandiji 46% i Grčkoj, 43,8%[11] i SAD 44% (populaciji belih Amerikanaca, starijih od 50 godina)[3,12]. Veća je u odnosu na brazilsku populaciju, starijih od 80 godina, koji borave u domovima za stare (29,2%)[10] i veća od učestalosti MS odraslih Republike Srpske (38,4%)[13].

Naši ispitanici su imali nižu učestalost MS u odnosu na stariju populaciju Brazila (47,9%-5,3%)[10], Republike Srpske (61,4%-64,9%)[13] i SAD (46,7%)[14]. U nekoliko istraživanja je utvrđeno da su lica starija od 70 godina imala MS od 42,6% do 70%, što je značajno više od naših nalaza i što odgovara starosti naših ispitanika[13,16,17].

U studiji koja je koristila tri različite definicije MS

Discussion

This research was performed on a relatively small sample of the older rural population and it revealed a high incidence of MS (42.7%) among outpatients. The incidence of MS among our participants is within MS prevalence range (22.3-69.7%)[10] of the elderly people and is similar to those of some Europian countries – Netherlands 46%, Greece 43.8% [11], USA 44% (the population of Caucasians, over 50 years of age)[3,12]. Nevertheless, it is higher than in Brasilians, over the age of 80, who live in the homes for the elderly (29.2%) or adults from the Republic of Srpska (38.4%).[13]

Our participants had lower MS incidence compared to the older population of Brasil (47.9%-50.3%)[10], Republic of Srpska (61.4%-64.9%)[13] and USA (46.7%)[14]. Several studies found that people over the age of 70, which is similar to our participants, had MS incidence of 42.6%-70%, which is high above the incidence of our participants.[15,16,17]

In the study, which used three different definitions of

(*IDF,* SZO i *NCEP*), učestalost MS kod muškaraca starosti od 50 do 59 godina bila je 38,9%, 35,5% i 29,7[18] i niža je nego u našoj studiji, ali u mlađoj i muškoj populaciji i pokazuje kolike razlike u učestalosti MS mogu da nastanu zbog primene različitih definicija MS. Ako posmatramo samo učestalost

MS kod naših pacijenata muškog pola (35,8%), ona je u potpunoj saglasnosti sa ovom studijom, a zbog visoke starosti naših ispitanika ova učestalost je, mada još uvek visoka, sasvim prihvatljiva.

Dosadašnja istraživanja su pokazala da učestalost MS raste sa godinama od 6,2% kod lica od 20 do 29 godina do 43,5% kod onih od 60 do 69 godina[4].

Smatra se da je visoka učestalost MS u starijih osoba posledica funkcionalnih i metaboličkih promena, koje su posledica starenja10.

Naše istraživanje je potvrdilo nalaze drugih studija da je učestalost MS veća kod žena (46,8%) nego kod muškaraca (35,8%), mada ta razlika nije bila statistički značajna, sa odnosom 1,3 prema 1 u korist žena[1,11,12,13], i u okviru je nalaza učestalosti MS drugih studija, koja varira od 8% do 43%, kod muškaraca, i od 7% do 56% kod žena[3].

Moreira i saradnici[15] nalaze značajno veću učestalost MS od naše kod žena (65,4%) nego kod muškaraca (34,6%), starije od 70 godina.

Istraživanja su pokazala da se učestalost MS kod žena u postmenopauzi povećava i da se kreće od 32,6% do 41,5%[2], što se može objasniti većom učestalošću abdominalne gojaznosti i niskog nivoa *HDL* holesterola, kod starijih žena, kao posledica menopauznih hormonskih promena koje povećavaju rizik za razvoj MS za 60%[10].

Naši rezultati pokazuju da su žene imale veće prosečne vrednosti indeksa telesne mase (*BMI*) i obima struka i manje vrednosti *HDL*, *LDL* holesterola i triglicerida u odnosu na muškarce, ali koje nisu statistički značajne. Jedina razlika je da su žene imale značajno veću koncentraciju ukupnog holesterola u poređenju s muškarcima.

Kod tumačenja rezultata treba istaći da u našoj kao i u drugim[15] studijama nije procenjivana interferencija antilipemičnih lekova, koje su upotrebljavali neki od ispitanika, na nivo lipida, što je moglo dati drugačiju sliku o njihovim vrednostima.

Naša studija je pokazala da je sa tri komponente MS bilo najviše ispitanika - 51,3% što je u saglasnosti sa nalazima drugih studija[19]. Od pojedinačnih komponenata najveću,preko 75% imali povišen krvni pritisak, povećan nivo šećera u krvi i triglicerida.

Uočljiva je neslaganje između učestalosti abdominalne gojaznosti i niskog nivoa *HDL* holesterola kod naših ispitanika. Poznato je da je kod gojaznih osoba snižen nivo *HDL* holesterola, ali da je za to odgovorna masa intraabdominalnog masnog tkiva, a ne ukupna masa masnog tkiva[13], što može objasniti trostruko veću učestalost abdominalne gojaznosti u odnosu na nivo niskog *HDL* holesterola kod naših pacijenata.

MS (IDF, WHO, NCEP), the incidence of MS, among men between the age 50-59, was 38.9%, 35.5% и 29.7%.[18] It was lower than in our study, but it took into account only men of the certain age and it revealed the extent of the differences in MS incidence, which may occur due to different MS definitions. If we only look at the MS incidence in our male participants (35.8%), then it`s quite consistent with this study, and due to the much older age of our participants, this incidence, although still high, is quite acceptable.

Up to date studies have shown that MS incidence increases with age, ranging from 6.2% in those 20-29 years of age to 43.5% in those 60-69.[4]

It is considered that the high incidence of MS in the elderly is due to the functional and metabolic changes that come with age.[10]

Our research confirmed the findings of other studies – MS incidence is higher in women (46.8%) than in men (35.8%), although the difference bore no statistical importance, with rate 1.3 to 1, for women.[1.11.12.13] Our findings are within the range of MS incidence of other studies, which vary from 8-43% for men and 7-56% for women.[3] *Moreira* [15] finds significantly higher MS incidence than ours, in women (65.4%) compared to men (34.6%), over the age of 70. The studies have shown that MS incidence increases in postmenopausal women and ranges from 32.6% до 41.5%.[2] A higher incidence of abdominal obesity and lower HDL cholesterol in older women, as a result of menopausal hormonal changes, accounts for this and increases the risk for MS for 60%.

Our results have shown women had higher mean BMI and waist circumference values, but lower HDL, LDL cholesterol and triglycerides, compared to men, but it bore no statistical significance. The only important difference was women had altogether higher levels of total cholesterol, compared to men. Interpreting the results we must stress that in our study, as well as other studies[15], interference of antilipemic drugs wasn`t assessed, and they were used by some participants, so they could have affected lipid levels in those participants.

Our study demonstrated three MS components were most frequent in our participants – 51.3%, which correlates to findings in other studies.[19] The most frequent singular MS component was waist circumference with 91.2%, but elevated blood pressure, glucose level, and triglycerides were also frequent with the incidence of 75%. The discrepancy between the frequency of abdominal obesity and low HDL cholesterol was rather noticeable among our participants. It is general knowledge, that obese people have got low HDL cholesterol due to the volume of intraabdominal fat, but not total body fats[13], which can explain for the three fold higher frequency of the abdominal obesity, compared to low levels of HDL cholesterol in our patients.

Pecanac[11] also finds abdominal obesity as the most frequent component of MS, followed by elevated blood pre-

Pećanac i saradnici[11] takođe nalaze abdominalnu gojaznost kao najučestaliju komponentu, a zatim povišen krvni pritisak i hiperglikemiju, a Lović i saradnici[9] najčešće hipertenziju u 79,7%, hiperglikemiju 72,8%, abdominalnu gojaznost u 62,7%, hipertrigliceridemiju u 58,0% i snižen *HDL* holesterol u 53,5%. Druge studije registruju kao najčešće komponente MS hiperglikemiju[3], hipertrigliceridemiju[6,11,20] ili povišen krvni pritisak[15,21]. Nizak nivo *HDL* holesterola bila je najčešća komponenta MS u 63,9% osoba starijih od 80 godina, što je dvostruko više u odnosu na učestalost niskog nivoa *HDL* holesterola u naših ispitanika[10].

Postojanje ovako značajnih razlika u učestalosti pojedinih komponenti MS, nastalih zbog upotrebe različitih kriterijuma u definiciji MS, posledica su razlika posmatranih populacija - da li je gradska ili seoska, zatim od pola, starosnog doba ili etničke pripadnosti, načina ishrane, nivoa fizičke aktivnosti, socioekonomskog stanja, obrazovanja i individualnih razlika u genetici[2].

Istraživanja *Montazerifar*-a i saradnika[20] su pokazala da je kod bolesnika sa koronarnom bolešću i MS najčešće nađen nizak nivo *HDL* holesterola - u 84,8%, hiperglikemije u 77,8%, povećan obim struka u 75,8%, i potvrđuju značaj niskog nivoa *HDL* holesterola kao faktora rizika koronarne bolesti[22] jer nivoi niskog *HDL* holesterola u opštoj populaciji, kao što je naša, nisu toliko učestali. To je potvrđeno ovom studijom koja je pokazala nisku učestalost koronarne bolesti (5,6%) i manju učestalost niskog nivoa *HDL* holesterola.

Naše istraživanje je utvrdilo da su osobe sa MS imale četiri puta veću učestalost infarkta miokarda i pet puta veću učestalost koronarne bolesti u odnosu na osobe bez MS, i potvrdilo značaj MS kao faktora rizika za razvoj koronarne bolesti, što je pokazano i u drugim istraživanjima[8]. U *Botnia studiji*[23] prisustvo MS je utrostručilo rizik za nastanak koronarne bolesti, a Finska prospektivna studija[24], koja je obuhvatila osobe starosti od 42 do 60 godina, pokazala je da prisustvo MS povećava rizik za nastanak koronarne bolesti više od četiri puta, što je u saglasnosti sa našim nalazima[11].

Druge studije nalaze da se rizik od razvoja koronarne bolesti povećava u prisustvu MS 7,3 puta kod muškaraca i 10,2 puta kod žena[3]. Ovo je u saglasnosti sa našim nalazima jer je učestalost koronarne bolesti naših ispitanika sa MS (10,5%) bila višestruko i značajno veća u odnosu na one bez MS (1,96%). Kod naših ispitanika prosečne koncentracije *LDL* holesterola bile su, neočekivano, značajno veće u osoba bez MS u odnosu na one sa MS, što indirektno ukazuje na značaj i potencijal uzajamnog dejstva komponenata MS, kao faktora rizika za razvoj ateroskleroze i koronarne bolesti.

Jedan od mogućih razloga nižih nivoa *LDL* holesterola kod naših pacijenata sa MS, može biti upotreba statina koji snižavaju *LDL* holesterol, datih kao primarna i sekundarna prevencija kardiovaskularnog rizika[25]. Potvrđeno je da su niske koncentracije *HDL* holesterola i visoki nivoi triglicerida poznati kao aterogena dislipidemija, kardiovaskularni faktor

ssure and hyperglycemia, while *Lovic*[9] finds hypertension in 79.7%, hyperglycemia in 72.8%, abdominal obesity in 62.7%, hypertriglyceridemia in 58.0% and low HDL cholesterol in 53.5% of the examinees.

Other studies registered hyperglycemia[3], hypertriglyceridemia[6,11,20] or elevated blood pressure[15,21] as the most frequent MS components. Low HDL cholesterol level was the most frequent MS component in 69.3% in people over 80 years of age, which is twice as much compared to our participants[10].

These significant differences in the frequency of MS components are due to not only the different criteria for the definition of MS, but are also the consequence of different observed populations, whether they live in the city or in the country, which gender they are, what age or ethnicity, what are their nutritional habits, level of physical activity, socioeconomic status, education and individual genetic variations.[2]

The research of *Montazerifar et al*[20] showed that in people with CAD and MS low HDL cholesterol was the most frequent 84.8%, followed by hyperglycemia 77.8% and increased waist circumference 75.8%, which solidifies the importance of low HDL cholesterol levels as the risk factor for CAD[22] , because the low levels of HDL cholesterol in the general population, such as ours, were less frequent. Our study confirmed the same, because there were few patients with CAD (5.6%), but also few patients had low HDL cholesterol.

Our study confirmed patients with MS had a four times higher incidence of myocardial infarction, and five times higher incidence of CAD, compared to patients without MS and thus confirmed the importance of MS as a risk factor for CAD. It was also shown in other studies.[8] Presence of MS triples the risk for CAD, *Botnia* study[23] showed, while the Finish prospective study[24], which included people from 42-60 years of age, showed MS increased the risk for CAD more than four times, which correlates to our findings.[11]

Other studies found the risk of CAD increasing 7.3 times in men and 10.2 times in women.[3] This correlates to our findings, because the incidence of CAD in our patients with MS (10.5%) was multiple times significantly higher, compared to those without MS (1.96%). Mean levels of LDL cholesterol were unexpectedly significantly higher in our participants without MS than in those with MS, which indirectly points out to the importance and potential of synergic effects of the components of MS, as risk factors for atherosclerosis and CAD.

One of the possible reasons for low LDL cholesterol levels in our patients with MS might be the use of statins (which lower LDL cholesterol), which were given for primary or secondary prevention of cardiovascular diseases.[25] It has already been confirmed that low levels of HDL cholesterol and elevated levels of triglycerides, also known as atherogenic dyslipidemia, are CV risk factors, inconsequential of the levels of LDL cholesterol.[25,26] Triglycerides, and not only

rizika bez obzira na nivo *LDL* holesterola[25,26], da su uzrokovane aterosklerozom, i da predskazuju nastanak koronarne bolesti nezavisno od nivoa ukupnog holesterola, *LDL* i *HDL* holesterola[11].

Uticaj pušenja kao faktora rizika na učestalost koronarne bolesti, kao i uticaj jedne ili dve komponente MS kod osoba bez MS, koji mogu značajno da utiču na razvoj koronarne bolesti, nismo pratili što treba uzeti u obzir.

Povezanost MS i koronarne bolesti pokazana je u studijama sa prisustvom visoke učestalosti MS među bolesnicima sa infarktom miokarda i ishemičnom kardiomiopatijom u 71%[11], bolesnika sa infarktom miokarda sa *ST* elevacijom u 54%[20] i potvrđeno u studijama sa visokom učestalošću MS među bolesnicima sa koronarnom bolešću u 49,5% do 60,0%[20,27]. To je potvrđeno i nedavnom studijom kod osoba sa utvrđenom bolešću koronarnih arterija, koja je pokazala da je učestalost MS u korelaciji sa stepenom vaskularnih lezija[12].

Viši kardiovaskularni rizik u MS posledica je aterosklerotskih promena[12]. Brojne studije su nesumnjivo pokazale da povećanje broja faktora rizika dovodi do ubrzanja procesa ateroskleroze, što se može objasniti činjenicom da upala uzrokovana MS ima važnu ulogu u ovom procesu[9]. Proinflamatorno stanje je direktno povezano sa uzrocima rezistencije na insulin, kao i aterogeneze (1,28). Smatra se da promene u koncentracijama inflamatornih biomarkera doprinose razvoju MS uglavnom kod starijih osoba. Starenje može kompromitovati imuni sistem, sa povećavanjem sinteze inflamatornih medijatora. Visoke koncentracije interleukina-6 (*IL*-6) faktora tumorske nekroze (*TNF*-α) i *C*-reaktivnog proteina (*CRP*),, povezani su sa komponentama MS[10].

Takođe, gojaznost i MS karakterišu pored prisustva supkliničke inflamacije i hipoadiponektinemija i poremećaj metaboličke homeostaze koji su istovremeno odgovorni za razvoj ateroskleroze kao nezavisnog prediktora kardiovaskularnih događaja[1,5,29,30].

Naše istraživanje je pokazalo da su osobe sa MS imale značajno veću smrtnost u odnosu na osobe bez MS, što je zapaženo i u drugim studijama, s tim da je taj odnos kod naših ispitanika bio višestruko veći od nalaza u drugim studijama, ali smrtnost nije izlazila izvan okvira opšte smrtnosti populacije našeg područja. Finska studija[24] je pokazala da prisustvo MS udvostručava nastanak ostalih uzroka smrti. Ovi nalazi potvrđuju da je MS značajan faktor povećane smrtnosti kod pacijenata sa MS u poređenju sa onim bez MS, kao i u poređenju sa nalazima drugih studija[2], ali da je, svakako, i posledica znatno starije populacije naših ispitanika u odnosu na ispitanike u drugim studijama. Rezultati nekih populacionih studija pokazuju da je MS koristan u predviđanju ukupnog kardiovaskularnog mortaliteta i da je kod osoba sa MS opšti mortalitet veći za 6%-7%, a kardiovaskularni za 12%-17%[5].

Relativno visoka učestalost MS u našoj studiji povezana je sa visokom učestalošću hipertenzije i dijabetesa kod naših ispitanika. Istraživanja pokazuju da je rasprostranjenost

cholesterol, are important risk factors for CVD and they are the predicament of CAD, independent of the levels of total, HDL and LDL cholesterol.[11]

The influence of smoking, as the risk factor for CAD, as well as the influence of one or two components of MS in patients without MS, which can significantly influence the development of CAD, haven`t been followed in our study and it should be taken into consideration.

The connection between MS and CAD was shown in the studies with a high prevalence of MS – among the patients with myocardial infarction and ischemic cardiomyopathy 71%[11], myocardial infarction with ST-elevation 54%[22] and coronary artery disease 49.5%-60%.[20,27] It was also confirmed in the recent study, in people with diagnosed CAD – the frequency of MS correlated to the degree of vascular lesions.[12]

Higher CV risk in MS is a consequence of atherosclerotic changes.[12] Numerous studies have proven, beyond a shadow of a doubt, that the increase in the number of risk factors leads to the acceleration of the atherosclerotic process, probably due to inflammation caused by MS.[9] Proinflammatory condition is in the direct connection with the causes of insulin resistance, as well as atherogenesis.[1,28]

Inflammatory biomarkers concentration changes are thought to be a prevailing factor in the development of MS, mainly in older people. Aging may compromise the immune system, by increased synthesis of inflammatory mediators. High concentrations of interleukin-6, tumor necrosis factor and C-reactive protein are connected with MS components.[10]

Obesity and MS are characterized, beside subclinical inflammation and hypoadiponectinemia, by metabolic homeostasis disorder, and at the same time they are responsible for the atherosclerosis onset as an independent predictor of CV events.[1.5.29,30]

Our study has shown that people with MS have significantly higher mortality than those without MS, which was confirmed in other studies as well, only in our study this ratio was multiple times higher than in other studies, but as far as mortality was concerned it was within mortality rates of the general population. Finish study[24] showed that the presence of MS doubles the appearance of other death causes. These findings confirm MS is an important factor for increased mortality in patients with MS, compared to those without MS, as well to findings of other studies[2], but it is also the consequence of the older age of our participants, compared to the participants in other studies. Results of some population studies show MS is useful in the prediction of the total CV mortality and in people with MS total mortality is 6%-7% higher, while cardiovascular is 12%-17% higher.[5]

Relatively high incidence of MS in our study correlates to a high incidence of hypertension and diabetes. Researches show the prevalence of MS in hypertensive patients is six times higher compared to those without hypertension, which

MS u hipertenzivnoj populaciji šest puta veća u odnosu na one bez hipertenzije, što ukazuje na jasnu povezanost hipertenzije i drugih faktora rizika za kardiovaskularne bolesti[15]. To je pokazano u studijama gde je nađena visoka učestalost MS u hipertenzivnoj populaciji u 61%, a u dijabetesnoj od 43,8% do 69,1%[31,32].

Mada ova studija obuhvata stariju i seosku populaciju, njeni rezultati se mogu proširiti i na druge populacione grupe i biti korisni u svakodnevnom radu lekara opšte medicine, posebno u prevenciji kardiovaskularnih oboljenja i dijabetesa[15].

Ovo istraživanje ukazuje da je neophodno razviti zdravstveni program kako bi se podstakao zdraviji stil života, poboljšale navike ishrane i fizičke aktivnosti, sa usklađenim preventivnim akcijama usmerenim na kontrolu svih komponeneta metaboličkog sindroma[28,33].

clearly points to the connection between hypertension and other CV risk factors.[15] There were studies which showed a high incidence of MS among hypertensive patients (61%) and in diabetic patients 43.8%-69.1%.[31,32]

Although our study includes older, rural population, its results can be extrapolated to other population groups and be found useful in GP`s everyday work especially in the field of CV and diabetes prevention.[15]

This research indicates health program should be developed to promote a healthier lifestyle, improve eating habits and entice physical activity, with concurrent preventive activities aiming at control of all MS components.[28,33]

Zaključak

Učestalost metaboličkog sindroma u populaciji ambulantnih pacijenata je 42,7%, muškaraca 35,8% i žena 46,8%. Slična je učestalosti u drugim zemljama i ne pokazuje značajne razlike između polova. Povećan obim struka je najčešća pojedinačna komponenta metaboličkog sindroma. Osobe sa metaboličkim sindromom imaju značajno veću učestalost koronarne bolesti i veći mortalitet, u odnosu na osobe bez metaboličkog sindroma, što ukazuje da je metabolički sindrom značajan faktor rizika za nastanak i razvoj koronarne bolesti i lošiju prognozu ovih osoba, zbog čega mora biti adekvatno kontrolisan efikasnom primarnom i sekundarnom prevencijom.

Conclusion

The incidence of metabolic syndrome in outpatients was 42.7%, of whom 35.8% were men and 46.8% women. It is similar to the incidence in other countries and there is no significant difference between genders. Increased waist circumference was the most frequent singular MS component. People with metabolic syndrome have a significantly higher incidence of CAD and higher mortality, compared to those without MS, which indicates MS is an important risk factor for onset and development of CAD, as well as worse prognosis in these people, so it needs to be under control with effective primary and secondary prevention.

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Primljen * Received 08.05.2019.
Prihvaćen * Accepted 15.07.2019.