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EFFECT OF SERUM LIPID LEVEL CHANGE ON 10-YEAR CORONARY HEART RISK DISTRIBUTION ESTIMATED BY MEANS OF SEVEN DIFFERENT CORONARY RISK SCORES DURING ONE-YEAR TREATMENT

UTICAJ PROMENA KONCENTRACIJE SERUMSKIH LIPIDA TOKOM JEDNOGODIŠNJEG LEČENJA NA PROMENU DISTRIBUCIJE 10-GODIŠNJEG RIZIKA ZA KORONARNU BOLEST SRCA PROCENJENU PRIMENOM SEDAM BODOVNIH SISTEMA

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Summary

Introduction. This study was done in order to evaluate the effect of serum levels of total cholesterol, triglycerides, low-density lipoprotein-cholesterol and high-density lipoprotein-cholesterol on 10-year coronary heart disease risk distribution change. **Material and Methods.** This study included 110 subjects of both genders (71 female and 39 male), aged 29 to 73, treated at the Outpatient Department of Atherosclerosis Prevention, Centre for Laboratory Medicine, Clinical Centre Vojvodina. The 10-year coronary heart disease risk was estimated on first examination and after one-year treatment by means of Framingham, PROCAM and SCORE coronary risk scores and their modifications (Framingham Adult Treatment Panel III, Framingham Weibul, PROCAM NS and PROCAM Cox Hazards). Age, gender, systolic and diastolic blood pressure, smoking, positive family history and left ventricular hypertrophy are risk factors involved in the estimation of coronary heart disease besides lipid parameters. **Results.** There were no significant differences in nutritional status, smoking habits, systolic and diastolic pressure, and no development of diabetes mellitus or cardiovascular incidents during one-year follow. However, a significant reduction in cholesterol level ($p<0.001$), triglycerides ($p<0.001$), low-density lipoprotein cholesterol ($p<0.001$) and an increase in high-density lipoprotein cholesterol ($p<0.02$) was present although therapeutic target values were not achieved. In addition, a significant increase was observed in the category of low 10-year coronary heart disease risk (Framingham- $p<0.001$; Framingham ATP III- $p<0.001$; Framingham Weibul- $p<0.001$; PROCAM– $p<0.05$; PROCAM NS- $p<0.05$; PROCAM Cox Hazards- $p<0.001$; SCORE- $p<0.001$) and a reduction in high-risk category (Framingham- $p<0.001$; Framingham ATP III- $p<0.005$; Framingham Weibul- $p<0.005$; PROCAM– $p<0.001$; PROCAM NS-$p<0.001$; PROCAM Cox Hazards- $p<0.001$; SCORE- $p<0.005$) in comparison with the risk at the beginning of the study. **Conclusion.** Our results show that the correction of lipid level after one-year treatment leads to a significant redistribution of 10-year coronary heart disease risk estimated by means of seven different coronary risk scores. This should stimulate patients and doctors to persist in prevention measures.

Key words: Coronary Disease; Cardiovascular Diseases; Serum; Lipids; Risk Factors; Male; Female; Adult; Middle Aged; Aged; Risk Assessment; Hyperlipidemias; Treatment Outcome

Sažetak

Uvod. Ovo istraživanje izvedeno je sa ciljem ispitivanja uticaja promena serumskih koncentracija ukupnog holesterola, triglicerida, holesterola u lipoproteinima male gustine i holesterola u proteinima velike gustine na promenu distribucije 10-godišnjeg rizika za koronarnu bolest srca. **Materijal i metode**. U ispitivanje je uključeno 110 ispitanika, 71 žena i 39 muškaraca, starosti 29−73 godine, upućenih u Ambulantu za prevenciju ateroskleroze Centra za laboratorijsku medicinu Kliničkog centra Vojvodine. Procena 10-godišnjeg koronarnog rizika vršena je bazalno i nakon godinu dana lečenja pomoću Framingamskog, PROCAM i SCORE bodovnog sistema i njihovih modifikacija (*Framingham ATP III*, *Framingham Weibul*, *PROCAM NS* i *PROCAM Cox Hazards*). Pored parametara lipidskog statusa, u procenu su uključeni: uzrast, pol, sistolni i dijastolni krvni pritisak, pušenje, porodična anamneza i hipertrofija leve komore. **Rezultati.** U posmatranom periodu nije došlo do signifikantnih promena stanja ishranjenosti ispitanika, broja pušača, sistolnog i dijastolnog pritiska, niti do razvoja šećerne bolesti i kardiovaskularnih incidenata. Međutim, ustanovljeno je signifikantno sniženje holesterola ($p < 0,001$), triglicerida ($p < 0,001$) i LDL holesterola ($p < 0,001$), a porast HDL-holesterola ($p < 0,02$), iako nisu uspostavljene ciljne terapijske vrednosti. Takođe, došlo je do signifikantnog povećanja kategorije niskog 10-godišnjeg koronarnog rizika (*Framingham* – $p < 0,001$; *Framingham ATP III* – $p < 0,001$; *Framingham Weibul* – $p < 0,001$; *PROCAM*– $p < 0,05$; *PROCAM NS* – $p < 0,05$; *PROCAM Cox Hazards* – $p < 0,001$; *SCORE* – $p < 0,001$) i sniženja kategorije visokog rizika (*Framingham* – $p < 0,001$; *Framingham ATP III* – $p < 0,005$; *Framingham Weibul* – $p < 0,005$; *PROCAM* – $p < 0,001$; *PROCAM NS* – $p < 0,001$; *PROCAM Cox Hazards* – $p < 0,001$; *SCORE* – $p < 0,005$), u odnosu na rizik na početku praćenja. **Zaključak.** Naši rezultati pokazuju da korekcija nivoa lipida nakon jednogodišnjeg lečenja dovodi do signifikantne preraspodele distribucije 10-godišnjeg rizika za koronarnu bolest srca procenjenog pomoću sedam različitih bodovnih sistema**.** To bi trebalo da stimuliše i bolesnike i doktore da istraju na merama prevencije.

Ključne reči: Koronarna bolest; Kardiovaskularne bolesti; Serum; Lipidi; Faktori rizika; Muško; Žensko; Odrasli; Odrasli, srednjih godina; Procena rizika; Hiperlipidemije; Ishod lečenja

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Abbreviations

CVD – cardiovascular diseases
CHD – coronary heart disease
LDL – low-density lipoprotein
HDL – high-density lipoprotein
sdLDL – small, dense low-density lipoprotein
MONICA – Multinational MONItoring of trends and determinants in CArdiovascular disease
BMI – body mass index

Introduction

Cardiovascular diseases (CVD), especially coronary heart disease (CHD) take a very high place among the leading causes of mortality worldwide and particularly in Eastern European countries. The standard mortality rate from cardiovascular diseases was 473.52 per 100.000 inhabitants in Serbia in 2011, thus Serbia is among those countries with high risk factors for CVD with fatal outcome in comparison with the average mortality rate in European Union countries of 212.85 per 100.000 inhabitants [1].

Lipids are among major independent risk factors for development of CHD and still have the central place in the majority of coronary risk scores for 10-year coronary heart disease estimation [2–6].

Lipids are important structural and bioregulatory components of human cell and plasmatic lipoprotein as their transportation circulatory forms. The low-density lipoprotein (LDL) fraction has the greatest atherogenic potential because its contribution to cholesterol accumulation in subendothelial layer of arterial blood vessels is dominant in comparison with other lipoproteins [3, 6]. On the contrary, high-density lipoprotein (HDL) has an antiatherogenic role in reducing cholesterol accumulation in the arterial wall [3] and the potential cardioprotective mechanism can be attributed to its antioxidative, antiinflammatory and antithrombotic activity [6–9]. Numerous studies have shown that triglycerides also have a significant role in atherogenesis and thrombogenesis independently from LDL and HDL levels through the potential of trygliceride-rich-lipoproteins within the reactions of reverse cholesterol transport and through the small, dense LDL (sdLDL) particle formation [6, 10, 11].

The correlation between the rate of atherosclerosis and lipid levels was confirmed in several, large, prospective, epidemiological studies such as Framingham study [12], PROCAM-Munster Heart Study [5,13] and SCORE study [4]. Other non-lipid parameters like age, smoking, hypertension, diabetes mellitus and positive family history for myocardial infarction in first line relatives before 60 years of age were also included in the estimation [4, 5, 12, 13]. Coronary risk scores have been designed as final results of data processing from these studies in order to identify asymptomatic persons at high risk for CHD development [14], and they include certain individual factors whose estimation provides a certain number of scores serving as a basis for expressing 10-year CHD risk in percents in a special table [4, 5, 12, 13]. Another way is to find the field for every single subject which would be closest to his/her age group, level of total cholesterol and systolic blood pressure and which already bears the number representing the percent of 10-year risk [15].

Framingham risk score (FRS) was designed in 1991 and risk factors incorporated in the estimation of risk were age, serum levels of total cholesterol, HDL cholesterol, systolic and diastolic blood pressure, presence of diabetes mellitus and smoking [12, 16]. In 2001, the National Cholesterol Education Program (NCEP) accepted and modified FRS for the guidebook "Adult Treatment Panel III (ATP III)" by changing its age intervals and excluding dyastolic blood pressure (Framingham ATP III risk score). There is a model suitable for use on computer and it is called Framigham Weibul, which assess the presence of the left ventricular hypertrophy, thus being different from other risk score systems [3, 17, 18].

PROCAM risk score scheme includes eight independent risk factors: age, LDL-cholesterol, HDL-cholesterol, triglycerides, systolic blood pressure, smoking, diabetes mellitus and positive family history for myocardial infarction in first line relatives before 60 years of age. This risk score refers only to men. The risk for females in menopause equals the risk for males divided by number four [5, 13, 18]. PROCAM NS modification has resulted from the data obtained from the Multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) project for the city of Novi Sad, which calculates the 10-year risk by multiplying the total sum of individual scores with the conversion factor 1.37 for men and 1.24 for women [18]. PROCAM *Cox proportional hazards model* is the modification adjusted for the computer use [18].

Risk factors included in the estimation of 10-year CHD risk according to SCORE risk scheme are gender, age, smoking, systolic blood pressure and total cholesterol. There are separate schemes for high- and low-risk regions for CHD as well as for males and females [15].

While the limit for high 10-years CHD risk is set at >20%, medium 10–20%, and low <10% in the majority of score systems, in the SCORE risk system it is >5%, 1-5%, <5%, respectively [4, 15, 19, 20].

Since lipids are in the central place of all coronary risk scores and their levels have a significant influence on a person's position in different risk categories, our investigation was carried out to evaluate the effect of changing lipid level on the distribution of 10-year CHD risk. The estimation was made basally and after one-year treatment by means of seven different risk score systems. These kinds of studies are very rare [21], practically non-existent in our region.

Material and Methods

This prospective, one-year study included 110 subjects of both genders (71 female and 39 male),

aged 29 to 73, without CHD or CHD equivalent disease (diabetes mellitus, peripheral arterial disease, abdominal aortic aneurism or carotid disease), who were examined and treated mainly for lipid metabolism disorder at the Outpatient Department of Atherosclerosis Prevention, Centre for Laboratory Medicine, Clinical Centre Voivodina.

The patients underwent measurements of body mass (kg), body height (cm) and arterial blood pressure (mmHg).

Blood pressure was measured by Riva-Rocci manometer in sitting position after 10-15 minutes rest [22].

Body height was measured by the Martin anthropometer with 0.1 cm precision, the subjects being barefoot, in standing position, their heels together and toes open, with the position of the head such as to make the Frankfurt plane (tragus line that connects the outer ears and ear angle) horizontal [22].

Body mass was measured by decimal scales with mobile weights and precision of 0.1 kg. The subjects were dressed, but 1 kg in summer and 1.5 kg in winter was subtracted on the account of their clothes [22].

Body waist circumference was measured in the middle between the lowest point of rib angle and the uppermost border of the iliac crest by the centimeter tape, with precision of 0.1 cm, the subjects being in standing position [22].

Body mass index (BMI) was calculated from the anthropometric parameters and the nutritional status was assessed according to the criteria of the World Health Organization (WHO) as well as national guideline for obesity [23,24].

In addition, the assessment was also made in relation to the presence of coronary heart disease electrocardiogram (ECG), diabetes mellitus (fasting glucose and glycated hemoglobin A_{1c} – HbA_{1c}) and lipid metabolism disorder (lipid parameters). Coronary heart disease was clinically evaluated and proved by the cardiologist (positive family history of cardiovascular events and/or angina pectoris and/or abnormal coronary angiogram).

The data were analyzed on first examination and after one-year treatment. The risk factors included in the estimation were age, gender, lipid parameters, blood pressure, positive family history, smoking, presence of diabetes mellitus and left ventricular hypertrophy. Each subject had their 10-year CHD risk calculated by applying seven different coronary risk score systems.

Within Framingham risk score, the estimation was done by means of the original, modified according to ATP III, and computer interactive Weibul model. PROCAM risk score system was used as a classical schematic model, a model adapted for computer called *Cox proportional hazards model,* and PROCAM NS. Ten-year CHD risk was estimated according to SCORE risk score system by means of the schemes for European regions at high risk.

Microsoft Excel 2003 was used to process the statistical data. The applied statistical functions included the arithmetic mean, standard deviation, percentage difference and Student T-test [25].

Results

The study sample consisted of 110 participants, of whom 39 (35.5%) were males and 71 (64.5%) were females, without clinical manifestations of atherosclerotic disease. Their average age was 54.5±10.1 years, BMI was 26.7±3.3 kg/m^2 and body waist was 87.5±11.8 cm. The average values of systolic and diastolic pressure were 131.1±15.4 and 82.3±9.1 mmHg, respectively and fasting glucose was 5.3 ± 0.7 mmol/l. Of the total number of participants, 18.2% were smokers and 43% of them had positive family history (**Table 1**).

Regarding the gender, women were significantly more present ($p<0.001$) and they were older ($p<0.02$) than men.

As for BMI, all subjects were overweight. There were no significant changes after one-year treatment.

The average values of systolic and diastolic blood pressures in males were 128.3±11.0 and 81.7±7.8 mmHg and in females 132.7±17.3 and 82.6±9.7 mmHg, respectively. The levels of fasting glucose were 5.4 ± 0.7 mmol/l and 5.3 ± 0.7 mmol/l in males and females, respectively. After one- year treatment, there were no significant differences in the levels of systolic and diastolic blood pressures and in fasting glucose levels, either in the whole study sample or in male and female subgroups. There were significantly fewer male smokers than female smokers (15% vs. 20%, $p<0.02$), with no significant reduction in the number of smokers after one-year treatment.

Positive family history for myocardial infarction in first line relatives was present in 31% of males and 49% of females.

Graphs 1 and 2 show the tested lipid parameters on first examination and after one-year treatment of lipid disorder. On first examination, the levels were as follows: total cholesterol - 7.29±1.41 mmol/l, triglycerides - 2.28±1.05 mmol/l, LDL-cholesterol - 5.07±1.33 mmol/l and HDL-cholesterol -1.23±0.37 mmol/l. After one-year treatment, the levels were: total cholesterol - 5.74±1.12 mmol/l, triglycerides - 1.48±0.73 mmol/l, LDL-cholesterol - 3.70±1.10 mmol/l and HDL-cholesterol - 1.35±0.37 mmol/l. Except HDL-cholesterol, which showed a significant increase after one-year treatment ($p<0.02$), a significant decrease in concentration of all other tested lipid parameters was recorded ($p<0.001$).

On first examination, the levels in males were: total cholesterol - 7.05±1.41 mmol/l, triglycerides - 2.30±1.03 mmol, LDL-cholesterol - 4.93±1.37 mmol/l and HDL-cholesterol - 1.08±0.24 mmol/l and in females they were: total cholesterol - 7.43±1.40 mmol/l, triglycerides - 2.25±1.07 mmol, LDL-cholesterol - 5.15±1.31 mmol/l and HDL-cholesterol - 1.31±0.39 mmol/l. After one-year treatment, the levels in males were: total cholesterol - 5.62±1.23

Table 1. Comparison of examined non-lipid risk factors on first examination and after one-year treatment
Tabela 1. *Poređenje ispitivanih nelipidskih faktora rizika prilikom prvog pregleda i nakon godinu dana lečenja*

	Total/*Ukupna grupa*		Males/*Muškarci*		Females/*Žene*	
	First examination *Prvi pregled*	After one year *Nakon godinu dana*	First examination *Prvi pregled*	After one year *Nakon godinu dana*	First examination *Prvi pregled*	After one year *Nakon godinu dana*
	x±SD	x±SD	x±SD	x±SD	x±SD	x±SD
Age (years)/*Starost*	54.5±10.1	-	51.1±11.4	-	56.2±9.1**	-
BMI (kg/m^2)	26.7±3.3	26.1±3.4	27.0±2.5	26.2±2.6	26.5±3.7	26.0±3.8
Body waist circumference (cm)/*Obim struka*	87.5±11.8	85.9±11.2	95.5±8.0	92.8±7.7	83.1±11.3	82.1±11.0
Systolic BP (mmHg) *Sistolni TA*	131.1±15.4	129.6±15.1	128.3±11.0	128.7±14.2	132.7±17.3	130.1±15.7
Diastolic BP (mmHg) *Dijastolni TA*	82.3±9.1	81.6±8.4	81.7±7.8	82.0±8.3	82.6±9.7	81.4±8.5
Fasting glucose (mmol/l) *Glikemija našte*	5.3±0.7	5.3±0.7	5.4±0.7	5.3±0.7	5.3±0.7	5.3±0.7
Smokers/*Pušači* (%)	18.2	16.4	15.4	15.4	19.7	16.9
Positive family history/ (%)*Pozitivna porodična istorija*	43	-	31	-	49	-

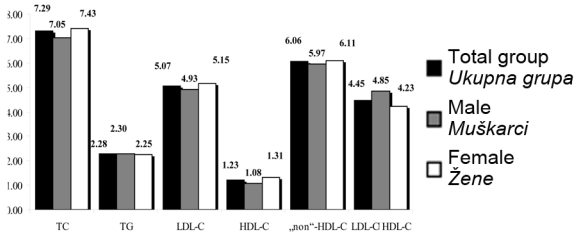
Legend: BP - blood pressure/*TA - krvni pritisak*; BMI - body mass index/*indeks telesne mase*; ** p<0.02

mmol/l, triglycerides - 1.50±0.76 mmol/l, LDL-cholesterol - 3.73±1.16 mmol/l and HDL-cholesterol - 1.21±0.31 mmol/l and in females they were: total cholesterol -5.81±1.06 mmol/l, triglycerides - 1.47±0.72 mmol/l, LDL-cholesterol - 3.69±1.08 mmol/l and HDL-cholesterol - 1.43±0.35 mmol/l. All tested lipid parameters, except HDL-cholesterol, were significantly reduced after one-year treatment (p<0.001). The levels of HDL-holesterol rose in males (p<0.05) while in females there were no significant changes. The levels of HDL-cholesterol were higher in females on first examination.

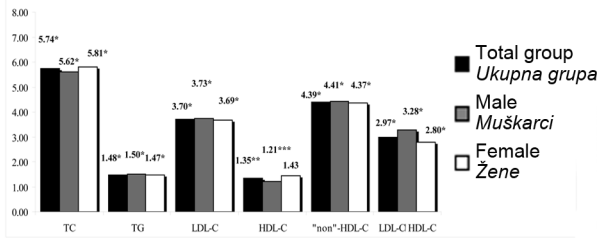
The application of seven different risk score systems for the estimation of 10-year coronary risk in the whole study sample on first examination showed that the percentage of subjects at low risk varied from 14.5% according to Framigham Weibul to 78.2% according to PROCAM; and after one-year treatment it was 39.1% to 88.2% according to PROCAM and Framingham Weibul, respectively. There was a significant increase in the number of subjects at low risk after one-year treatment according to all tested risk score systems (**Table 2**).

In the intermediate-risk category group, the percentage of subjects was from 11.8% according to PROCAM NS to 45.4% according to Framigham Weibul and after one-year treatment there were 10.0% according to PROCAM and 36.4% according to Framigham Weibul. The reduction in number of persons having intermediate risk was significant only according to Framnigham, Framingham ATP III and PROCAM Cox Hazards (**Table 2**).

On first examination, the percentage of persons at high risk in the whole study sample varied from 8.2% according to PROCAM to 40.0% ac-



Graph 1. Lipid parameters on first examination
Grafikon 1*. Parametri lipidskog statusa pri prvom pregledu*
Legend (*legenda*): Total group (*ukupna grupa*), males (*muškarci*), females (*žene*), TC - Total cholesterol (*ukupan holesterol*); TG – triglycerides (*trigliceridi*); C – cholesterol (*holesterol*)



Graph 2. Lipid parameters after one-year treatment
Grafikon 2. *Parametri lipidskog statusa nakon godinu dana lečenja*
Legend (*legenda*): Total group (*ukupna grupa*), males (*muškarci*), females (*žene*) TC - Total cholesterol (*ukupan holesterol*); TG – triglycerides (*trigliceridi*); C – cholesterol (h*olesterol*); * - p<0.001; **- p<0.02; *** - p<0.05

Table 2. Estimation of 10-year CHD risk by means of coronary risk score on first examination and after one-year treatment
Tabela 2. *Procena 10-godišnjeg rizika za koronarnu bolest srca prlikom prvog pregleda i nakon godinu dana lečenja*

	PP (FE)	NG (AY)		PP (FE)	NG (AY)		PP (FE)	NG (AY)	
	Low risk/*Nizak rizik*			Medium risk/*Srednji rizik*			High risk/*Visok rizik*		
	%	%	p<	%	%	p<	%	%	p<
Framingham	38.2	68.2	0.001	43.6	25.4	0.001	18.2	6.4	0.001
Framingham ATPIII	54.5	78.2	0.001	31.8	15.4	0.001	13.6	6.4	0.005
Framingham Weibul	14.5	39.1	0.001	45.4	36.4	n.s.	40.0	24.5	0.005
PROCAM	78.2	88.2	0.05	13.6	10.0	n.s.	8.2	1.8	0.001
PROCAM NS	74.4	85.5	0.05	11.8	10.9	n.s.	13.6	3.6	0.001
PROCAM Cox Hazards	63.6	83.6	0.001	25.4	13.6	0.005	10.9	2.7	0.001
SCORE	43.6	55.4	0.001	33.6	32.7	n.s.	22.7	11.8	0.005

Legend/*legenda*: FE - first examination/*PP - prvi pregled*, AY - after one year/NG − *nakon godinu dana lečenja*, n.s.− non-significant/*nesignifikantno*

Table 3. Estimation of 10-year CHD risk by means of coronary risk score on first examination and after one-year treatment in males
Tabela 3*. Procena 10-godišnjeg rizika za koronarnu bolest srca prlikom prvog pregleda i nakon godinu dana lečenja kod muškaraca*

	PP (FE)	NG (AY)		PP (FE)	NG (AY)		PP (FE)	NG (AY)	
	Low risk/*Nizak rizik*			Medium risk/*Srednji rizik*			High risk/*Visok rizik*		
	%	%	p<	%	%	p<	%	%	p<
Framingham	33.3	56.4	0.002	43.6	28.2	n.s.	23.1	15.4	n.s.
Framingham ATPIII	28.2	51.3	0.05	43.6	30.8	n.s	28.2	17.9	n.s.
Framingham Weibul	17.9	41.0	0.025	51.3	35.9	n.s	30.8	23.1	n.s.
PROCAM	38.4	66.6	0.02	38.5	28.2	n.s	23.1	5.1	0.001
PROCAM NS	28.2	59.0	0.01	33.3	30.8	n.s	38.5	10.3	0.001
PROCAM Cox Hazards	25.6	56.4	0.005	43.6	35.9	n.s	30.7	7.7	0.001
SCORE	35.9	46.1	n.s.	25.6	28.2	n.s	38.6	25.6	n.s.

Legend/*legenda*: FE - first examination/*PP - prvi pregled*, AY - after one year/NG − *nakon godinu dana lečenja*, n.s.− non-significant/*nesignifikantno*

Table 4. Estimation of 10-year CHD risk by means of coronary risk score on first examination and after one-year treatment in females
Tabela 4. *Procena 10-godišnjeg rizika za koronarnu bolest srca prlikom prvog pregleda i nakon godinu dana lečenja kod žena*

	PP (FE)	NG (AY)		PP (FE)	NG (AY)		PP (FE)	NG (AY)	
	Low risk/*Nizak rizik*			Medium risk/*Srednji rizik*			High risk/*Visok rizik*		
	%	%	p<	%	%	p<	%	%	p<
Framingham	49.3	74.6	0.005	35.2	23.9	n.s.	15.5	1.4	0.001
Framingham ATPIII	69.0	93.0	0.001	25.4	7.1	0.001	5.6	0	n.s.
Framingham Weibul	12.7	38.0	0.001	42.2	36.6	n.s.	45.1	25.3	0.005
PROCAM	100	100	n.s.	0	0	n.s.	0	0	n.s.
PROCAM NS	100	100	n.s.	0	0	n.s.	0	0	n.s.
PROCAM Cox Hazards	84.5	98.6	0.005	15.5	1.4	0,001	0	0	n.s.
SCORE	47.9	60.6	n.s.	38.0	35.2	n.s.	14.1	4.2	0.001

Legend/*legenda*: FE - first examination/*PP - prvi pregled*, AY - after one year/NG − *nakon godinu dana lečenja*, n.s.− non-significant/*nesignifikantno*

cording to Framingham Weibul. After one-year treatment, that percentage was 1.8% according to PROCAM and 24.5% according to Framingham Weibul. The reduction was significant according to all seven risk score systems (**Table 2**).

The percentage of male subjects having low risk was from 17.9% according to Framingham Weibul to 38.4% according to PROCAM, and after one-year treatment, it was from 41.0% to 66.6% according to PROCAM and Framingham Weibul, respectively. After one-year treatment, there was a significant rise in the number of male subjects with low risk according to all risk score systems, except SCORE (**Table 3**).

In the intermediate-risk category, the reduction was not significant, while in the high-risk category, a significant reduction was present only according to all PROCAM risk score systems (**Table 3**).

The application of score systems for estimating 10-year coronary risk showed that the low risk category in the female subgroup of the study sample varied from 12.7% according to Framingham Weibul up to 100% according to PROCAM, while after one-year treatment, it was from 38.0% to 100%. Significant differences were not present only when PROCAM, PROCAM NS and SCORE were applied (**Table 4**).

In the intermediate risk category, the significant differences were present only when Framingham ATP III and PROCAM Cox Hazards were applied, while in the high risk category, they were recorded when Framingham, Framigham Weibul model and SCORE were applied as well (**Table 4**).

Discussion

Numerous epidemiological studies have shown that lipids are the most important risk factor and the obligatory parameter of all 10-year coronary risk score systems, which have been or should be included in routine clinical work. Numerous interventional studies have also suggested that the correction of lipid level leads to absolute or relative coronary heart risk reduction. However, until the year of 2009 and *the IMPROVE-dyslipidemia study* conducted by Hatzitolios et al. [21], there were no literature data about the significance of lipid level reduction on the distribution of 10-year CHD risk estimated by means of coronary risk score systems.

The Guideline for Diagnosis and Treatment of Lipid Disorders issued in 2011 recommended the application of SCORE system in our country [26]. However, since none of these score systems is ideal in prediction, the decision was to apply two other mostly used coronary risk scores Framingham (original, modified according to ATP III and computer Weibul model) and PROCAM (original, modified according to MONICA and computer Cox Hazards model) besides SCORE in our research. No literature data are available on such a global estimation of risk score systems. In *the IMPROVE-dyslipidemia study* [21], Framingham and PROCAM risk scores were applied for the estimation; while in *Co-Laus* study [27], the original Framigham scores and the one recalibrated for Swiss population were used. Similar studies used Framingham and SCORE [28], only Framingham [29] or just PROCAM [30] risk score schemes in our population. Unlike our research, which included subjects with dyslipidemia, other studies performed on our population included randomly selected participants from the general population and the effect of lipid level correction was not estimated.

Our study sample consisted of 110 subjects, 39 males and 71 females, aged 29 to 73 years, the women being older than men as in *the IMPROVE-dyslipidemia* [21] and *Co-Laus* study [27]. Positive family history of myocardial infarction in the first generation before 60 years of age, incorporated as a risk factor in PROCAM risk score, was positive in 45% of subjects in *the IMPROVE-dyslipidemia study* [22] and in 43% of our study sample. The percentage of smokers in our study sample was 18.2%, that being significantly lower than in *the IMPROVE-dyslipidemia study* (45%), and unlike *Co-Laus* study, the number of female smokers was higher than of the male smokers [21, 27].

At the beginning of our research, the serum lipid levels of total cholesterol, triglycerides and LDL-cholesterol were higher than in the previously mentioned studies [27–31], except in *the IMPROVE-dyslipidemia study* because this study was done on dyslipidemic patients and the effect of lipid level correction was estimated after six-month treatment [21]. After one-year treatment, a significant correction of all examined lipid parameters was found in our patients, so the total cholesterol was 5.74 mmol/l, triglycerides - 1.48 mmol/l, LDL-cholesterol - 3.70 mmol/l, while the level of protective HDL-cholesterol rose to 1.35 mmol/l. In *the IMPROVE-dyslipidemia study* the lipid parameters were also significantly corrected after six-month treatment [21].

It can be noticed that at the beginning of our research there were great percentage differences in risk category distribution for 10-year CHD risk calculated by means of seven different CHD risk score systems. Our results suggest that Framingham Weibul model has the most severe classification criteria in female participants. According to it, 45.1% of female subjects are at high risk for CHD, while that percentage is 0-15.5% according to other examined CHD risk score systems. In men, however, SCORE and PROCAM Cox Hazards have the most severe criterion, the percentage distribution of high risk individuals being 38.6% and 38.5%, respectively. It can also be concluded that PROCAM has the mildest criteria in both males and females. The distribution of low CHD risk in males was 38.4% and in females almost 100%, so PROCAM in females is practically useless since it underestimates the risk for CHD due to a very rough approxima-

tion [17]. In *Co-Laus* study [27], *the IMPROVE-dyslipidemia study* [21] as well as in the study conducted by Jovičić et el. [28], the percentage of low risk individuals estimated by means of the applied coronary risk score systmes was significantly higher than in our research.

Although target therapeutic values were not reached [26] after one-year treatment of dyslipidemia, a significant reduction in 10-year CHD risk was achieved according to all score systems applied in the research. Namely, a statistically significant increase in the number of participants at low risk was observed, as well as the decrease in the number of participants having intermediate and high risk. A significant increase in the low risk category was present in the whole study sample and in men according to all score systems, which were applied; whereas, in women it was present in all three Framingham risk scores as well as in PROCAM Cox Hazards. A statistically significant reduction in the high CHD risk category was recorded by all CHD risk score systems in the whole study sample; whereas in men it was recorded by all three PROCAM risk scores and in women by Framingham, Framingham Weibul and SCORE.

Bearing in mind that all CHD risk scores include one or two lipid parameters in their algorithm, these data are in accordance with the correction of tested parameters of lipid status after one-year treatment of our patients. It is similar to *the IMPROVE-dyslipidemia* study, where the total risk reduction was 63% according to Framingham and 45% according to PROCAM risk score [21].

Conclusion

The results of this investigation show that the reduction of total cholesterol, triglycerides, low-density lipoprotein-cholesterol and the increase in levels of high-density lipoprotein-cholesterol have a significant influence on total 10-year coronary heart disease risk reduction. This shows that the application of coronary risk score systems in everyday routine clinical practice would be useful not only for the identification of asymptomatic persons at high risk of developing coronary heart disease and the selection of initial therapy in their treatment but also during the course of treatment, periodically as a confirmation of a positive therapeutic effect. The application of coronary risk score systems could also have a motivational role for patients. It is necessary to correct not only lipids but also other risk factors that can be changed.

References

1. WHO Global Database [Internet]. [cited 2013 December 7]. Available from: http://data.euro.who.int/hfadb/.

2. Ostojić M. Recommendations for prevention of ishemic heart disease. 1st ed. Beograd: Ministarstvo zdravlja Republike Srbije; 2002. Serbian.

3. The Expert Panel. The third report of the national cholesterol education program (NCEP), Expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Tratment Panel III) final report. Circulation 2002;106:3143-421.

4. De Backer G, Ambrosioni E, Borch-Johansen K, Brotons C, Cifkova R, Dallongeville J, et al. European guidelines on cardiovascular disease prevention in clinical practice: third joint task force of European and other societies on cardiovascular disease prevention in clinical practise. Eur J Cardiovas Prev Rehabil. 2003;10(Suppl 1):S1-10.

5. International task force for prevention of coronary heart disease. Pocket guide to prevention of coronary heart disease. 1st ed. Grunnwald: Börm Bruckmerer Verlag GmbH; 2003.

6. Đerić M, Stokić E, Vučković B, Kojić-Damjanov S, Čabarkapa V. Lipids and atherosclerosis. Jugoslov Med Biohem 2006;25(4):325-31.

7. Zuliani G, Vigna GB, Fellin R. The anti-atherogenic properties of HDL particles. International Congress Series 2007;1303:103-10.

8. Zhnag Q, Ling L, Xiao-Yan Z. Protective roles of HDL, apoA-I, and mimetic peptide on endothelial function: through endothelial cells and endothelial progenitor cells. Int J Cardiol. 2009;133:286-92.

9. Tsompanidi EM, Brinkmeier MS, Fotiadou EH, Giakoumi SM, Kypreos KE. HDL biogenesis and functions: role of HDL quality and quantity in atherosclerosis. Atherosclerosis 2010;208:3-9.

10. Rizzo M, Berneis K. Low-density lipoprotein size and cardiovascular risk assessment. QJM 2006;99(1):1-14.

11. Shin HK, Kim YK, Kim KY, Lee JH, Hong KW. Remnant lipoprotein particles induce apoptosis in endothelial cells by NAD(P)H oxidase-mediated production of superoxide and cytokines via lecitin-like oxidized low-density lipoprotein receptor-1 activation: prevention by cilostazol. Circulation 2004;109:1022-8.

12. Boston: Framingham Heart Study. Boston: National Hearth Lung and Blood Institute [Internet], [cited 2013 December 7]. Available from: (http://www.framinghamheartstudy.org/about-fhs/index.php).

13. Assman G, Cullen P, Shulte H. Simple scoring scheme for calculating the risk of acute coronary events bazed on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study. Circulation 2002;105:310-5.

14. Grundy SM, Cleeman JI, Mertz NB, Brewer B, Clark L, Hunninghake D, et al. Implications of recent clinical trials for National Cholesterol Education Program Adult Treatement Panel III Guidelines. J Am Coll Cardiol 2004;44(3):720-32.

15. Graham I, Atar D, Borch-Johansen K, Boysen G, Burrel G, Cifkova R, et al. European guidelines on cardiovascular disease prevention in clinical practice. Eur J Cardiovas Prev Rehabil 2007;14(Suppl 2):S1-113.

16. Savić T. Evaluation, diagnosis and treatment of dyslipidemia. 1st ed. Niš: Medicinski fakultet Univerziteta u Nišu; 2004 (In Serbian).

17. Grundy SM. Approach to lipoprotein management in 2001. National Cholesterol Guidelines. Am J Cardiol 2002;8 (Suppl 1):11-21.

18. International task force for prevention of coronary heart disease. [Internet] [cited 2013 December 7]. Available from: http://www.chd-taskforce.com.

19. Conroy RM, Pyörälä K, Fitzgerald AP, Sams S, Menniotti A, Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE Project. Eur Heart J 2003;24:987-1003.

20. Erhardt LR, Gotto A. The evolution of European guidelines: changing the management of cholesterol levels. Atherosclerosis 2006;185(1):12-20.

21. Hatzitolios AI, Athyros VG, Karagiannis A, Savopoulos C, Charalambous C, Kyriakidis G, et al. Implementation of strategy for management of over dyslipidemia: the IMPROVE-dyslipidemia study. Int J Cardiol 2009;134:322-9.

22. Tomić-Naglić D. Total and visceral fat mass in evaluation of cardiovascular risk at obese women [Magistarska teza]. Novi Sad: Medicinski fakultet; 2006. Serbian.

23. Micić D. Obesity. 1st ed. Beograd: Ministarstvo zdravlja Republike Srbije; 2004. Serbian.

24. WHO, Global database on body mass index [Internet]. [cited 2013 December 7]. Available from: http:// www.who.int/bmi/index.jsp?introPage=intro_3.htlm.

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25. Grujić V, Jakovljević Đ. Application of statistics in medical research. Novi Sad: Medicinski fakultet Novi Sad; 1998. Serbian.

26. Zamaklar M. Nacionalni vodić dobre kliničke prakse za dijagnostifikovanje i lečenje lipidskih poremećaja. Beograd: Agencija za akreditaciju zdravstvenih ustanova; 2012.

27. Marques-Vidal P, Rodondi N, Bochud M, Chiolero A, Pecoud A, Hayoz D, et al. Predictive accuracy of original and recalibrated Framingham risk score in the Swiss population. Int J Cardiol. 2009;133:346-53.

28. Jovičić S, Ignjatović S, Majkić-Singh N. Comparison of two different methods for cardiovascular risk assessment: Framingham risk score and score system. Jugoslav Med Biohem. 2007;26(2):94-7.

29. Vekić J, Topić A, Zeljković A, Jelić-Ivanović Z, Spasojević-Kalimanovska V. LDL and HDL subclasses and their relationship with Framingham risk score in middle-aged Serbian population. Clin Biochem 2007;40:310-6.

30. Stefanović A, Kotur-Stevuljević J, Spasic S, Vekić J, Bujisić N. Association of oxidative stress and paraoxonase status with PROCAM risk score. Clin Biochem. 2009;42:617-23.

31. Petrović V, Jašarević Komljenović Z, Srdić B, Stokić E. Faktori rizika za razvoj kardiovaskularnih bolesti kod radnika Doma zdravlja u Beočinu. Med Pregl. 2008;61(5-6):257-62.