Indeks tjelesne mase kod bolesnika s pozitivnom dijagnozom ili sumnjom na koronarnu arterijsku bolest: veliko hrvatsko kohortno istraživanje

Body mass index in patients with positive or suspected coronary artery disease: a large Croatian cohort

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Sažetak

Uvod: Indeks tjelesne mase (engl. *body mass index*, BMI) jedna je od mjera koje se rabe u kliničkim epidemiološkim istraživanjima, kao i kod postavljanja kliničke dijagnoze pretilosti. Pretilost i BMI shvaćaju se kao nezavisni čimbenici rizika za nastanak koronarne arterijske bolesti (engl. *coronary artery disease*, CAD). Suprotno tomu, postoji mogućnost da nema povezanosti između BMI i CAD te ponekad može doći do „paradoksa pretilosti". Cilj ovoga istraživanja bio je utvrditi raspodjelu BMI kod bolesnika s područja Hrvatske s potvrđenom dijagnozom koronarne arterijske bolesti ili sa sumnjom na nju.

Ispitanici i metode: U istraživanju je sudjelovalo 728 bolesnika s područja Hrvatske koji su bili podvrgnuti koronarnoj angiografiji. Koncentracije glukoze, parametara lipidnog statusa, homocisteina i fibrinogena određene standardnim metodama. BMI se izračunao nakon mjerenja tjelesne mase i visine.

Rezultati: Nije bilo značajne razlike između triju kategorija BMI bolesnika s CAD(+) i CAD(-), niti između bolesnika koji su/nisu imali šećernu bolest ili su/nisu pušači. U skupini CAD(+) nije bilo povezanosti između infarkta miokarda (engl. *myocardial infarction*, MI) i BMI, no u toj je skupini bilo bitno više pretilih bolesnika s arterijskom hipertenzijom ($P = 0{,}005$). Iako statistički bitne, razlike koncentracije kolesterola ($P = 0{,}001$), HDL kolesterola ($P < 0{,}001$), apolipoproteina A-I ($P < 0{,}001$) i triglicerida ($P = 0{,}002$) u plazmi između bolesnika s normalnom tjelesnom masom, prekomjernom tjelesnom masom i onih pretilih bile su klinički nevažne. Nisu primijećene nikakve bitne uzajamne veze između HDL kolesterola, Apo A-I, triglicerida i hipertenzije s jedne te BMI s druge strane.

Zaključak: Kod bolesnika s pozitivnom dijagnozom CAD ili sa sumnjom na CAD BMI nije povezan s koronarnom arterijskom bolesti, kao ni s ostalim čimbenicima rizika koji su ispitani u ovoj studiji, s iznimkom hipertenzije.

Ključne riječi: indeks tjelesne mase; koronarna arterijska bolest; čimbenici rizika

Abstract

Background: BMI is one of the measures used in clinical epidemiological studies as well as in clinical diagnosis of obesity. Obesity and BMI have been implicated as independent risk factors for CAD. On contrary, the relationship between BMI and CAD may be absent or sometimes shows the "obesity paradox". The aim of the study presented was to determine the distribution of BMI in Croatian patients with confirmed or suspected coronary artery disease.

Materials and methods: 728 Croatian patients who underwent coronary angiography were involved in the study. The concentrations of glucose, lipid parameters, homocysteine and fibrinogen were determined with standard methods. BMI was calculated after measurement of body weight and height.

Results: There were no significant differences between three BMI-categories for CAD(+) and CAD(-) patients, neither for the patients with and without diabetes or smokers/non-smokers. In CAD(+) group, there was no relation between myocardial infarction (MI) and BMI, but there was significantly more obese patients with arterial hypertension ($P = 0.005$). Though statistically significant, differences in plasma cholesterol ($P = 0.001$), HDL-cholesterol ($P < 0.001$), apolipoprotein A-I ($P < 0.001$) and triglyceride ($P = 0.002$) concentrations between normal, overweight and obese patients were clinically irrelevant. No significant correlations were observed between HDL-cholesterol, Apo A-I, triglycerides and hypertension with BMI.

Conclusions: In patients with positive or suspected coronary artery disease, BMI is not associated with CAD or with other studied CAD-risk factors with the exception of hypertension.

Key words: body mass index; coronary artery disease; risk factors

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Uvod

Indeks tjelesne mase (engl. *body mass index*, BMI) prepoznat je, prema kriterijima Svjetske zdravstvene organizacije (SZO), kao uobičajeni čimbenik rizika za mnoge bolesti, uključujući koronarnu arterijsku bolest (engl. *coronary artery disease*, CAD), karcinom i šećernu bolest (1). Broj pretilih ljudi i ljudi s prekomjernom tjelesnom masom diljem svijeta u razvijenim i nerazvijenim zemljama raste strelovitom brzinom i poprima epidemijske razmjere zbog neravnoteže između prehrane i tjelesne aktivnosti (2). Inzulinska rezistencija, povišene koncentracije parametara metabolizma lipida u krvi i poremećaj u simpatičkom živčanom sustavu dovode se u vezu s pretilosti (3). Spoj inzulinske rezistencije, središnje pretilosti, hipertenzije i dislipidemije naziva se metaboličkim sindromom i predstavlja značajan čimbenik rizika za razvoj CAD (4,5). BMI se često rabi kao jedna od mjera u kliničkim epidemiološkim istraživanjima, kao i kod kliničke dijagnoze pretilosti. Pretilost se navodi kao nezavisan čimbenik rizika za nastanak CAD. Međutim, mnoga istraživanja opovrgavaju tu tvrdnju i ukazuju na činjenicu da ne postoji veza između BMI i CAD (6). Štoviše, čini se da je BMI slab čimbenik za dijagnozu pretilosti, budući da ne pravi razliku između postotka tjelesne masne i mišićne mase (7). Neka populacijska istraživanja pokazala su postojanje „paradoksa pretilosti" (6) ili ukazala na to da pretilost može biti „negativni predskazatelj" CAD (8). Ta su nas ranije provedena istraživanja potakla da ispitamo učestalost povišenog BMI u bolesnika iz Hrvatske kod kojih je potvrđena CAD ili se sumnja na nju i koji su bili podvrgnuti koronarnoj angiografiji.

Ispitanici i metode

Ispitanici

U istraživanje je bilo uključeno 728 bolesnika (498 muškaraca i 230 žena) koji su prošli koronarnu angiografiju u Specijalnoj bolnici za kardiovaskularnu kirurgiju i kardiologiju „Magdalena" u Krapinskim Toplicama. Uzorci krvi sakupljani su u razdoblju od 2001. do 2004. godine. Bolesnicima je dijagnosticirana CAD (nakon infarkta miokarda i/ili prethodne koronarne angiografije i/ili koronarne intervencije) ili su bili naručeni za koronarnu angiografiju zbog sumnje na koronarnu bolest na osnovi kliničke slike (tipična (stabilna) angina, pozitivan EKG stres test). Bolesnici s akutnim koronarnim sindromom (nestabilna pektoralna angina, akutni infarkt miokarda) isključeni su iz ovog istraživanja. Sakupljeni su i klinički podaci poput dobi, spola, težine, visine, statusa pušenja, prisutnosti šećerne bolesti, hipertenzije i infarkta miokarda. Svakom je bolesniku izmjerena masa i visina, a podaci o pušenju dobiveni su iz upitnika. Prethodni infarkt miokarda definiran je medicinskom dokumentacijom koja sadrži podatke o hospitalizaciji; promjenama na EKG (STEM ili NSTEM) i pri-

Introduction

Body mass index (BMI) has been recognized as a common risk factor for many diseases, including coronary artery disease (CAD), cancer and diabetes, according to the World Health Organization (WHO) criteria (1). The proportion of overweight and obese people increases to epidemic proportions in both industrialized and developing countries worldwide, because of imbalance between nutrition and physical activity (2). Insulin resistance, increased lipid parameters and disturbances in the sympathetic nervous system are associated with obesity (3). The association of insulin resistance, central obesity, hypertension and dyslipidemia is denoted as metabolic syndrome and presents a major risk factor for development of CAD (4,5). BMI is one of the measures often used in clinical epidemiological studies as well as in clinical diagnosis of obesity. Obesity has been implicated as an independent risk factor for CAD. However, many recent studies confute this statement and indicate the absence of controversial relationship between BMI and CAD (6). Moreover, BMI seems to be a poor diagnostic factor in obesity, because it does not discriminate between the percentage of body fat and lean mass (7). Some population studies have demonstrated the presence of "obesity paradox" (6) or indicate that obesity may be a "negative predictor" of CAD (8).
These previously reported observations encouraged us to explore the distribution of BMI in Croatian patients with confirmed or suspected CAD that underwent coronary angiography.

Subjects and Methods

Subjects

The study included 728 patients (498 male and 230 female) that underwent coronary angiography at "Magdalena" Specialized Hospital for Cardiovascular Surgery and Cardiology in Krapinske Toplice. Blood samples were collected from 2001 to 2004. The patients were diagnosed with known CAD (after myocardial infarction and/or previous coronary angiography and/or coronary intervention), or were scheduled for coronary angiography for suspected coronary disease based on clinical presentation (typical angina, positive stress test). Patients with acute coronary syndrome (unstable angina pectoris, acute myocardial infarction) were excluded from the study. Clinical data such as age, gender, weight, height, smoking status, diabetes mellitus, evidence of hypertension and myocardial infarction were collected. Body weight and height were measured in each patient and smoking status data were collected by use of a questionnaire. Previous myocardial infarction was defined on the basis of medical documentation on hospitalization for this diagnosis as defined by clinical symptoms, ECG changes (STEMI or NSTEMI) and

sutnošću povišenih biokemijskih biljega nekroze miokarda. Biokemijske analize vrednovane su najmanje mjesec dana nakon akutnog infarkta miokarda. Arterijska hipertenzija definirana je kao krvni tlak iznad 140/90 mm Hg izmjeren u više navrata bez antihipertenzivnog liječenja ili kao normalan krvni tlak izmjeren u ispitanika koji koriste antihipertenzivnu terapiju. Šećerna je bolest definirana prema koncentraciji glukoze u krvi [SZO kriterij (9)] i/ili primanju terapije inzulinom ili oralnim hipoglikemicima. Budući da su svi bolesnici bili naručeni za neobvezatnu koronarnu angiografiju, znači da nije bilo kliničkih simptoma ni znakova i/ili laboratorijskih rezultata koji bi ukazivali na akutnu infekcijsku bolest; bolesnici s poznatim zloćudnim bolestima nisu bili uključeni u ovo istraživanje. Ispitanici su podijeljeni u dvije skupine: 1) 468 ispitanika CAD(+) s minimalno 50%-tnom stenozom bilo koje od većih srčanih arterija i 2) 260 ispitanika CAD(-) s manje od 10%-tnom stenozom većih srčanih arterija. BMI se izračunavao nakon mjerenja tjelesne mase i visine. Bolesnici su nadalje podijeljeni u tri skupine prema BMI izraženom u kg/m^2: normalni, BMI < 25 kg/m^2 (BMI-1); s prekomjernom težinom, BMI 25–29 kg/m^2 (BMI-2); i pretili, BMI ≥ 30 kg/m^2 (BMI-3). Bolesnici su dali obaviješteni pristanak za sudjelovanje u istraživanju koje je odobrilo Etičko povjerenstvo Specijalne bolnice za kardiovaskularnu kirurgiju i kardiologiju „Magdalena" i Medicinskog fakulteta Sveučilišta u Zagrebu.

Metode

Uzorci krvi sakupljani su ujutro natašte. Koncentracije glukoze, triglicerida, ukupnog kolesterola i HDL kolesterola (nakon selektivne precipitacije na uređaju Immuno AG, Beč, Austrija) u plazmi mjerene su standardnim enzimatskim metodama na uređaju Olympus AU 640 (Olympus, Tokio, Japan). Koncentracija LDL kolesterola izračunala se pomoću Friedewaldove formule. U slučajevima kad je koncentracija triglicerida bila veća od 3 mmol/L, koncentracija HDL kolesterola mjerila se metodom direktne imunoinhibicije (Olympus Diagnostica, Lismeehan, Irska), a LDL kolesterola homogenim testovima (Randox Laboratories, Crumlin, Ujedinjeno Kraljevstvo). Koncentracija apolipoproiteina izmjerena je metodom nefelometrije na uređaju Dade Behring BN II (Dade Behring, Marburg, Njemačka). Koncentracija CRP je određena imunoturbidimetrijom na Olympusu AU 800 (Olympus, Tokio, Japan). Koncentracija homocisteina je određena pomoću FPIA na uređaju Imx-Abbott (Abbot Laboratories, Abbott Park, SAD). Modificirana Claussova metoda na uređaju BFA-Dade Behring (Dade Behring, Marburg, Njemačka) korištena je za mjerenje koncentracije fibrinogena.

Statističke analize

Statistička analiza je načinjena programskim sustavom za obradu podataka STATISTICA 7 (StatSoft, Inc 2003, SAD). Frekvencije CAD u podskupinama BMI određene su di-

presence of elevated biochemical markers of myocardial necrosis. Biochemical analyses were assessed at least a month after acute myocardial infarction. Arterial hypertension was defined as repeatedly observed blood pressure values of more than 140/90 mm Hg without antihypertensive therapy, or as normotensive blood pressure measurements under antihypertensive therapy. Diabetes mellitus was defined according to blood glucose values [WHO diagnostic criteria (9)] and/or presence of insulin or oral hypoglycemic therapy. All patients were scheduled for elective coronary angiography, implying that there were no clinical symptoms or signs and/or laboratory values indicative of acute infectious disease; patients with known malignancies were not included in this study. Study subjects were divided into two groups: 1) 468 CAD(+) subjects with at least 50% stenosis of any of the major coronary arteries; and 2) 260 CAD(-) subjects with less than 10% stenosis of major coronary arteries. BMI was calculated after body weight and height measurements. Patients were also divided into three groups according to BMI (in kg/m^2) as follows: normal, BMI < 25 kg/m^2 (BMI-1); overweight, BMI 25–29 kg/m^2 (BMI-21); and obese, BMI ≥ 30 kg/m^2 (BMI-3). Study patients signed an informed consent to participate in the study. The study was approved by Ethics Committees of the "Magdalena" Specialized Hospital for Cardiovascular Surgery and Cardiology and of Zagreb University School of Medicine.

Methods

Blood samples were collected after an overnight fast. Plasma concentrations of glucose, triglycerides, total cholesterol and HDL-cholesterol (after selective precipitation with Immuno AG, Vienna, Austria) were measured by standard enzymatic methods on an Olympus AU-640 (Olympus, Tokyo, Japan). LDL-cholesterol was calculated using Friedwald equation. If triglyceride concentration was above 3 mmol/L, HDL- and LDL-cholesterol were measured by direct immunoinhibition method (Olympus Diagnostica, Lismeehan, Ireland) and homogeneous assay (Randox Laboratories, Crumlin, United Kingdom), respectively. Apolipoproteins were measure by nephelometric methods on a Dade Behring BN II (Dade Behring, Marburg, Germany). CRP was determined by immunoturbidimetry on an Olympus AU 800 (Olympus, Tokyo, Japan). Homocysteine was determined by FPIA on an IMx-Abbott (Abbott Laboratories, Abbot Park, USA) device. Modificated Clauss method on BFA-Dade Behring (Dade Behring, Marburg, Germany) was used for the measurement of fibrinogen.

Statistical analysis

Statistical data analysis was performed by use of the STATISTICA 7 software (StatSoft, Inc., 2003,USA). CAD and BMI group frequencies were calculated by direct counting.

rektnim brojanjem. Kategoričke varijable uspoređene su pomoću Pearsonova χ^2-testa. Normalno raspodijeljene kontinuirane varijable izražene su kao $\bar{x} \pm$ SD uz 95%-tni interval pouzdanosti. Kontinuirane varijable koje nisu pokazivale normalnu raspodjelu izražene su kao medijani uz odgovarajuće interkvartilne raspone. Usporedbe kontinuiranih varijabla među skupinama napravljene su Studentovim t-testom ili Mann-Whitneyevim testom. Primijenjena je multivarijatna analiza varijance (MANCOVA) s dobi i spolom kao kovarijablama za testiranje učinka kategorije BMI na krvne parametre i broj zahvaćenih krvnih žila. Dobivene vrijednosti triglicerida, fibrinogena i broja zahvaćenih krvnih žila logaritamski su transformirane za multivarijatnu analizu varijance. Korelacije su dobivene izračunavanjem Pearsonova korelacijskog koeficijenta ili Spearmanovom korelacijom ranga. Razina značajnosti bila je manja od 0,05.

Rezultati

U tablici 1. prikazane su općenite značajke ispitanika u dvjema kliničkim podskupinama (bolesnici angiografski

Categorical variables were compared using Pearson's χ^2-test. Continuous variables with normal distribution were expressed as $\bar{x} \pm$ SD and 95% confidence interval (95% CI). Continuous variables without normal distribution were expressed as median and interquartile range. Group comparisons of continuous variables were performed by Student's t-test or Mann-Whitney test. Multivariate analysis (MANCOVA) with age and gender as covariates was used to test the BMI category effect on blood parameters and number of vessels affected. Values of triglycerides, fibrinogen, and number of vessels were log-transformed for multivariate analysis. Correlations were performed by calculating Pearson correlation coefficient or Spearman rank correlation. The level of significance was set at 0.05.

Results

Table 1 presents general characteristics of study subjects in two clinical subgroups (patients with and without angiographically confirmed CAD). As published previously, the well known risk factors for CAD, i.e. higher prevalence of male gender, cigarette smoking, diabetes, hyper-

Tablica 1. Značajke ispitanika prema rezultatima koronarne angiografije

Table 1. Characteristics of study subjects according their results of coronary angiography

	CAD (-), N = 260		CAD (+), N = 468		P value
Gender (male) (N, %)	152 (58.5 %)		346 (73.9 %)		**< 0.001**
Smoking (N, %)	67 (25.8 %)		180 (38.5%)		**0.001**
Diabetes (N, %)	21 (8.1 %)		94 (20.1%)		**< 0.001**
Hypertension (N, %)	126 (48.5 %)		271 (57.9 %)		**0.016**
Myocardial infarction (N, %)	/		257 (54.9 %)		/
	Mean ± SD	**95% CI**	**Mean ± SD**	**95% CI**	**P value**
Age (yrs)	57 ± 11	55–58	61 ± 10	60–62	**< 0.001**
Cholesterol (mmol/L)	5.81 ± 1.21	5.66–5.96	5.81 ± 1.43	5.68–5.94	0.952
HDL-cholestrol (mmol/L)	1.21 ± 0.32	1.17–1.24	1.09 ± 0.30	1.06–1.12	**< 0.001**
LDL- cholestrol (mmol/L)	3.80 ± 1.10	3.70–3.92	3.82 ± 1.29	3.70–3.93	0.868
Apo A-I (g/L)	1.43 ± 0.31	1.39–1.47	1.31 ± 0.28	1.28–1.34	**< 0.001**
Apo B (g/L)	1.14 ± 0.28	1.10–1.17	1.16 ± 0.33	1.13–1.19	0.287
Homocysteine (μmol/L)	12.38 ± 3.80	11.92–12.84	13.66 ± 4.91	13.2–14.09	**< 0.001**
BMI (kg/m^2)	27.71 ± 3.84	27.24–28.18	27.85 ± 3.81	27.51–28.21	0.627
	Median	**Range**	**Median**	**Range**	**P value**
Triglycerides (mmol/L)	1.49	0.43–1.73	1.83	0.27–10.85	**<0.001**
Fibrinogen (g/L)	2.80	1.10–7.70	3.10	0.80–12.80	**0.038**
Vessels (n)	/	/	2	1–7	/

The frequencies of categorical variables were tested with Pearson chi-square test. Comparison of continuous variables between two subject groups was done using the Student's t-test for age, BMI, lipids (except for triglycerides), apolipoproteins and homocysteine. Data were expressed as mean ± SD and 95% confidence interval (95% CI). Mann-Whitney test was used on comparison of triglycerides and fibrinogen. Data were expressed as median and interquartile range.
CAD – coronary artery disease; BMI – body mass index

potvrđenom CAD i bez nje). Kao što je i prije objavljeno, dobro poznati čimbenici rizika za razvoj CAD bili su znatno učestaliji kod skupine CAD(+), npr. muški spol, pušenje, šećerna bolest, hipertenzija, kao i više koncentracije triglicerida i homocisteina u plazmi te niža koncentracija HDL kolesterola. Učestalost pojavljivanja kategorija BMI raspodijeljenih prema osnovnim značajkama ispitanika prikazana je u tablici 2. Nije bilo značajnije razlike među trima kategorijama BMI ovisno o prisustvu CAD, šećerne bolesti ili statusu pušenja. U skupini bolesnika s CAD(+) nije bilo povezanosti između infarkta miokarda i BMI, no bilo je znatno više pretilih bolesnika s arterijskom hipertenzijom (P = 0,005). Koncentracije nekih biokemijskih parametara za tri kategorije BMI u skupini CAD(+) prikazane su u tablici 3. Multivarijatna analiza varijance s dobi i spolom kao kovarijablama pokazala je statistički značajne razlike

tension, as well as higher plasma concentrations of triglycerides and homocysteine, and lower HDL-cholesterol concentration, were significantly overrepresented in CAD(+) group. Frequencies of BMI categories according to baseline characteristics of study subjects are presented in Table 2. There were no significant differences in the three BMI categories either between CAD(+) and CAD(-) patients, patients with and without diabetes or according to their smoking status. In CAD(+) group, there was no correlation between myocardial infarction and BMI, but there were significantly more obese patients with arterial hypertension (P = 0.005). Concentrations of plasma parameters in CAD(+) group according to three BMI categories are shown in Table 3. Multivariate analysis with age and gender as covariates yielded significant differences in plasma cholesterol (P = 0.001), HDL-cholesterol

Tablica. 2. Učestalost kategorija BMI i osnovne značajke ispitanika

Table 2. Frequencies of body mass index (BMI) categories and baseline characteristics of study subjects

	BMI-1	BMI-2	BMI-3	P value*
All study subjects (N = 728)				
CAD (-)	61 (23.5 %)	135 (51.9 %)	64 (24.6%)	0.985
CAD (+)	112 (23.9 %)	243 (51.9 %)	113 (24.1 %)	
Diabetes (-)	152 (24.8 %)	318 (51.9 %)	143 (23.3 %)	0.193
Diabetes (+)	21 (18.3%)	60 (52.5%)	34 (29.6%)	
Hypertension (-)	92 (27.8 %)	175 (52.9 %)	64 (19.3 %)	**0.005**
Hypertension (+)	81 (20.4 %)	203 (51.1 %)	113 (28.5 %)	
Smoking (-)	117 (24.3 %)	250 (52.0 %)	114 (23.7 %)	0.816
Smoking (+)	56 (22.7 %)	128 (51.8 %)	63 (25.5 %)	
Subjects with CAD (N = 468)				
Male	75 (21.7 %)	189 (54.6%)	82 (23.7 %)	0.091
Female	37 (30. 3%)	54 (44.3 %)	31 (25.4 %)	
Infarct (-)	47 (22.3%)	111 (52.6%)	53 (25.1%)	0.731
Infarct (+)	65 (25.3%)	132 (51.4%)	60 (23.3%)	
Diabetes (-)	95 (25.4%)	195 (52.1%)	84 (22.5%)	0.143
Diabetes (+)	17 (18.1%)	48 (51.1%)	29 (30.9%)	
Hypertension (-)	54 (27.4%)	107 (54.3%)	36 (18.3)	**0.031**
Hypertension (+)	58 (21.4%)	136 (50.2%)	77 (28.4%)	
Smoking (-)	70 (24.3%)	150 (52.1%)	68 (23.6%)	0.934
Smoking (+)	42 (23.3%)	93 (51.7%)	45 (25.0%)	
No. of vessels (1)	33 (19.6 %)	93 (55.4 %)	42 (25.0 %)	
No. of vessels (2)	46 (31.3 %)	61 (41.5 %)	40 (27.2 %)	**0.025**
No. of vessels (3 and more)	33 (21.6 %)	89 (58.2 %)	31 (20.3 %)	

* Pearson's χ^2-test

Tablica 3. Biokemijski parametri i broj krvnih žila u skupini CAD(+) prema kategorijama BMI

Table 3. Biochemical parameters and number of vessels in CAD(+) group according to body mass index (BMI) categories

	BMI-1 (N = 112)	BMI-2 (N = 234)	BMI-3 (N = 113)	P value*
Age	62 ± 9	61 ± 10	59 ± 9	0.131
Cholesterol (mmol/L)	5.77 ± 1.27	5.85 ± 1.51	5.76 ± 1.41	**0.001**
HDL-chol. (mmol/L)	1.16 ± 0.36	1.07 ± 0.28	1.04 ± 0.26	<0.001
LDL-chol. (mmol/L)	3.81 ± 1.12	3.86 ± 1.37	3.73 ± 1.27	0.134
Apo A-I (g/L)	1.34 ± 0.32	1.31 ± 0.27	1.28 ± 0.26	<0.001
Apo B (g/L)	1.15 ± 0.30	1.17 ± 0.34	1.16 ± 0.35	0.182
Homocysteine (μmol/L)	13.95 ± 5.36	13.81 ± 5.07	13.00 ± 4.02	0.057
Triglycerides (mmol/L)	1.79 ± 1.00	2.10 ± 1.14	2.24 ± 1.17	0.002
Fibrinogen (g/L)	3.15 ± 1.13	3.24 ± 1.21	3.15 ± 1.13	0.134
Vessels (N)	2.07 ± 0.90	2.12 ± 1.12	1.96 ± 0.90	0.249
Glucose (mmol/L)	6.02 ± 2.68	6.07 ± 2.86	6.16 ± 2.76	0.980

* BMI category effect on blood parameters and number of vessels affected was performed using multivariate analysis with age and gender as covariates. Triglycerides, fibrinogen, and number of vessels were log-transformed for multivariate analysis.

u koncentracijama kolesterola (P = 0,001), HDL kolesterola (P < 0,001), apolipoproteina A-I (P < 0,001) i triglicerida (P = 0,002) između bolesnika s normalnom težinom, onih s prekomjernom težinom i pretilih bolesnika. Međutim, te razlike nisu bile klinički značajne, jer su se ispitivani parametri lipida razlikovali za manje od 5%. Korelacija između BMI i raznih parametara prikazana je u tablici 4. Niti jedan od ispitivanih parametara (HDL kolesterol, Apo A-I, triglicerida i hipertenzija) nije bio u korelaciji s BMI.

(P < 0.001), apolipoprotein A-I (P < 0.001) and triglyceride (P = 0.002) concentrations among normal, overweight and obese patients. Although significant, these differences were clinically irrelevant, because the difference between lipid parameters concentrations was less than 5%. Correlations between BMI and different parameters are presented in Table 4. None of the parameters tested (HDL-cholesterol, Apo A-I, triglycerides and hypertension) showed correlation with BMI.

Tablica 4. Korelacija između BMI (kg/m2) i drugih ispitanih parametara u skupini CAD(+)

Table 4. Correlation between body mass index (BMI; kg/m2) and other parameters in CAD(+) group

Correlated to BMI (kg/m²)	Total		Male		Female	
	R	P value	R	P value	R	P value
Cholesterol*	0.03	0.522	0.01	0.928	0.10	0.289
HDL-cholesterol*	-0.13	0.005	-0.16	0.002	-0.06	0.501
Apo A-I*	-0.09	0.049	-0.11	0.051	-0.05	0.618
Homocysteine*	-0.08	0.074	-0.09	0.113	-0.10	0.249
Age*	-0.06	0.152	-0.09	-0.081	0.01	0.891
	ρ	P value	ρ	P value	ρ	P value
Triglycerides**	0.16	<0.001	0.19	0.001	0.12	0.192
Vessels (N)**	-0.05	0.242	-0.09	0.106	0.02	0.822
Diabetes**	0.08	0.070	0.02	0.716	0.25	0.007
Hypertension**	0.10	0.023	0.12	0.026	0.08	0.402

*Pearson's correlation coefficient
**Spearman's rank correlation

Rasprava

Naše je istraživanje pokazalo slab dijagnostički doprinos BMI u određivanju rizičnih čimbenika za CAD, budući da nije ustanovljena veza između CAD i BMI. Iako se čini da BMI nije nezavisan čimbenik rizika za CAD, moguće je da je povezan s drugim čimbenicima rizika za CAD, kao što su npr. hipertenzija, šećerna bolest i koncentracija nekih lipidnih parametara. Nekoliko istraživanja novijeg datuma pokazala su kako ne postoji veza između CAD i BMI. U istraživanju provedenom na bolesnicima iz Austrije koji su prošli koronarnu angiografiju nije pronađena pozitivna veza između CAD i BMI (10). Štoviše, isti autori napominju da bi tjelesna masna masa mogla povećati broj srčanih krvnih žila s stenozom većom od 50%. Istraživanje provedeno u Italiji pokazalo je obrnutu povezanost između CAD i BMI kod pretilih bolesnika, dok se za CAD činilo da je povezana s odnosom opsega struka i bokova (engl. *waist to hip ratio*, WHR), ali samo kod bolesnika koji ne boluju od šećerne bolesti i imaju normalnu tjelesnu masu (11).

Mnoga nedavno objavljena istraživanja naglašavaju neočekivane i proturječne rezultate o vezi između BMI i CAD. U bolesnika iz SAD bilo je više angiografski normalnih srčanih arterija kod bolesnika sa sistoličkim srčanim zatajenjem koji su imali viši BMI (12). U jednoj američkoj studiji je postojanje „paradoksa pretilosti" utvrđeno među bolesnicima koji su prošli koronarnu angiografiju (6,13). Sistematični pregled različitih kohortnih istraživanja pokazao je kako kod bolesnika s nižim BMI i CAD postoji povećani dugoročni rizik smrtnosti u usporedbi s bolesnicima s normalnim BMI. Kod bolesnika s jako visokim BMI ukupni rizik smrtnosti nije povećan (14).

Prospektivno međunarodno istraživanje INVEST provedeno na više od 22.000 bolesnika s CAD i hipertenzijom upućuje na zaštitni učinak pretilosti zbog smanjenog rizika od primarnog ishoda i od ukupne smrtnosti (15). Istraživanje provedeno na više od 95.000 uzastopnih bolesnika podvrgnutih perkutanoj koronarnoj intervenciji u državi New York pokazalo je nižu bolničku smrtnost i veće neželjene popratne srčane reakcije kod pretilih bolesnika. Suprotno tomu, bolesnici s ekstremnim BMI (i oni s preniskom tjelesnom masom i oni s BMI iznad 40 kg/m^2) imali su znatno višu smrtnost (16). Bolesnici iz Kine s karcinogenskim šokom nakon što su preživjeli akutni infarkt miokarda imali su znatno niži BMI nego oni koji su preživjeli AMI, a nisu pretrpjeli karcinogenski šok (17).

Ispitivanje u kojem su sudjelovali bolesnici s CAD iz brojnih američkih bolnica objasnilo je jedan aspekt paradoksa pretilosti (18). Steinberg i sur. bilježe kako je skupina bolesnika s CAD i višim BMI bila mlađe dobne skupine, pretežito muškog spola, te su imali hipertenziju, šećernu bolest i hiperlipidemiju. Isti autori navode kako se viši BMI vjerojatno može povezati s boljom primjenom preporučenog medicinskog liječenja i invazivnog praćenja

Discussion

Our study showed poor diagnostic performance of BMI in the assessment of risk factors for CAD, because no relationship between CAD and BMI was demonstrated. Although BMI doesn't seem to be an independent risk factor for CAD, it may be related to some other CAD risk factors like hypertension, diabetes and plasma concentrations of some lipid parameters. Several recent studies showed no relationship between CAD and BMI either. A study including Austrian patients that underwent coronary angiography failed to detect any positive association of CAD and BMI (10). Moreover, the same authors suggest that body fat may increase the number of coronary vessels with > 50% stenosis. In obese Italian patients, BMI correlated inversely with CAD, while CAD appeared to be associated with the waist to hip ratio, however, only in nondiabetic patients with normal body weight (11).

Many recent studies have reported unexpected and controversial results concerning relationship between BMI and CAD. Angiographically normal coronary arteries were more prevalent in the USA patients with systolic heart failure and elevated BMI (12). The existence of "obesity paradox" was recorded in patients undergoing coronary angiography in the US study group (6,13). Systematic review of different cohort studies showed patients with low BMI and CAD to have an increased long-term mortality risk when compared with patients with normal BMI, whereas total mortality risk was not increased in patients with very high BMI (14).

A prospective international INVEST study in more than 22,000 patients suffering from CAD and hypertension suggested a protective effect of obesity due to decreased risks of primary outcome and all-cause mortality (15). A study in more than 95,000 consecutive patients from New York State that underwent percutaneous coronary intervention showed lower in-hospital mortality and higher rate of adverse cardiac events in obese patients. On the contrary, patients with extreme BMI (underweight and those with BMI over 40 kg/m^2) had a significant higher mortality (16). Chinese patients with carcinogenic shock after AMI had a significantly lower BMI than those that survived AMI without carcinogenic shock (17).

A study including CAD patients from numerous American hospitals explained one aspect of the obesity paradox (18). Steinberg *et al*. found the study group of CAD patients with higher BMI to be younger but more likely to be men and have hypertension, diabetes and hyperlipidemia. In the same study, higher BMI appeared to be associated with better use of the recommended medical therapy and invasive CAD therapeutic monitoring. This may have explained the lower rate of in-hospital mortality. A study carried out at Mayo Clinic showed overweight and obese individuals to be paradoxically protected from

terapije za CAD. To bi moglo objasniti nižu smrtnost kod hospitaliziranih bolesnika. Ispitivanje na Klinici Mayo pokazalo je da su nakon preboljenog akutnog infarkta miokarda ispitanici s prekomjernom tjelesnom masom i pretili ispitanici paradoksalno zaštićeni od kratkoročne smrti, no da kod njih postoji dugoročni rizik od smrtnosti koji je sličan onome kod ispitanika s normalnom tjelesnom masom (19).

Kvantitativnim određivanjem epikardijalnog masnog tkiva i perikoronarne masne mase pomoću kompjutorizirane tomografije u bolesnika iz Nizozemske pokazalo se da je količina masnog tkiva koja okružuje srčane arterije povezana s pretilošću i metaboličkim sindromom u bolesnika kod kojih postoji klinička sumnja na CAD (20). Nakupljanje perikardijalnog masnog tkiva bilo je snažniji čimbenik rizika za CAD nego drugi čimbenici raspodjele tjelesne masne mase kod nepretilih muških ispitanika iz Japana (21). Morricone i sur. nisu našli vezu između CAD i BMI. Zanimljivo je njihovo zapažanje da je CAD u uzajamnoj vezi s količinom visceralnog masnog tkiva kod bolesnika iz Italije koji nemaju šećernu bolest ili poremećaj tolerancije glukoze (22). Podaci iz studije Dallas Heart pokazuju da je omjer opsega struka i bokova nezavisno povezan s prevalencijom ateroskleroze i omogućava bolju diskriminaciju negoli BMI i opseg struka (23). Istraživanje provedeno na ukupno 27.098 ispitanika s AMI i kontrolnih ispitanika iz 52 zemlje, koje je obuhvatilo nekoliko velikih etničkih skupina, pokazalo je da je omjer opsega struka i bokova u izrazitoj vezi s rizikom od AMI diljem svijeta. Autori su zaključili da WHR daje točniju procjenu onih AMI koji se mogu pripisati pretilosti nego BMI (24).

Sva su ova saznanja pokazala da su omjer opsega struka i bokova, visceralno, epikardijalno te perikoronarno masno tkivo puno relevantniji pokazatelji pretilosti u procjeni čimbenika rizika za nastanak CAD, nego što je to BMI. Kako smo ovdje izložili, rezultati mnogih istraživanja pokazali su da nema povezanosti između BMI i kardiovaskularne bolesti. Podaci iz našega istraživanja također su pokazali nepostojanje korelacije indeksa tjelesne mase s CAD, kao ni sa šećernom bolesti, infarktom miokarda, statusom pušača, dobi i spolom. Nasuprot tomu, više slučajeva hipertenzije među pretilim bolesnicima (BMI ≥ 30 kg/m^2) ukazuje na to da bi i hipertenzija, kao dobro poznat čimbenik rizika, mogla biti povezana s BMI. Iako je statistička analiza lipidnih parametara među različitim podskupinama BMI pokazala značajnu razliku u regresijskom modelu prilagođenom prema dobi i spolu, dislipidemija se ne može tumačiti kao klinički značajna, jer su zapažene razlike bile manje od 5%.

Možemo zaključiti da je ispitivanje pokazalo kako ne postoji veza između BMI i CAD, kao ni između BMI i ostalih čimbenika rizika za CAD, s iznimkom hipertenzije. Mnoga nedavno provedena istraživanja predstavila su postojanje „paradoksa pretilosti". Ta ispitivanja ukazuju na to da

short-term death after AMI, but had a long-term mortality risk similar to normal weight individuals (19).

Quantitative determination of epicardial adipose tissue and pericoronary fat using by computed tomography in Dutch patients showed the amount of adipose tissue surrounding coronary arteries to be related with obesity and metabolic syndrome in patients clinically suspected of CAD (20). Pericardial fat accumulation was a stronger coronary risk factor than other factors of body fat distribution in non-obese Japanese men (21). Morricone *et al*. found no relationship between CAD and BMI. Interesting was their finding that CAD correlated with the amount of visceral adipose tissue in Italian patients without diabetes or impaired glucose tolerance (22). Data from the Dallas Heart Study showed the waist to hip ratio to be independently associated with prevalent atherosclerosis and provided better discrimination than either BMI or waist circumference (23). A case-control study of acute myocardial infarction that included 27,098 patients from 52 countries, representing several major ethnic groups, showed the waist to hip ratio to be highly significantly associated with the risk of myocardial infarction risk worldwide. The authors conclude that the waist to hip ratio provides better estimate of myocardial infarction attributable to obesity than BMI (24).

All these findings show the waist to hip ratio, visceral adipose tissue, epicardial adipose tissue and pericoronary fat to be more relevant obesity parameters in the evaluation of CAD risk factors than BMI. As discussed above, results of many studies point to the lack of association between BMI and cardiovascular disease. Our data also showed absence of BMI correlation with CAD as well as with diabetes, myocardial infarction, smoking status, age and gender. On the contrary, the higher prevalence of hypertension among obese patients (BMI ≥30 kg/m^2) suggested that hypertension as a well known factor may be associated with BMI. Although statistical analysis of lipid parameters among normal, overweight and obese patients showed significant differences in the corrected model, dyslipidemia could not be interpreted as clinically relevant because the observed differences were less than 5%.

In conclusion, the present study showed absence of the relationship between BMI and CAD, as well as between BMI and other CAD risk factors, with the exception of hypertension. Many recent studies pointed to the existence of the "obesity paradox". These studies suggest that scientists should be more careful in the interpretation of BMI and selection of study patients. Some other body fat indicators might be more relevant parameters in the evaluation of CAD risk factors than BMI.

znanstvenici moraju biti pažljiviji pri tumačenju BMI, kao i kod odabira bolesnika koji će sudjelovati u istraživanjima. Neki drugi pokazatelji masnog tkiva mogli bi biti važniji parametri za procjenu čimbenika rizika za CAD nego što je to BMI.

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