

Interrelation between the relative fat mass index and other obesity indices in predicting clinical severity and prognosis of acute myocardial infarction

Marko Mornar Jelavic^{1,2}, Zdravko Babic^{3,4,5}, Hrvoje Pintaric^{2,6}

¹Institute for Cardiovascular Prevention and Rehabilitation, Zagreb, Croatia

²School of Dental Medicine, University of Zagreb, Zagreb, Croatia

³School of Medicine, University of Zagreb, Zagreb, Croatia

⁴Faculty of Kinesiology, University of Zagreb, Zagreb, Croatia

⁵Coronary Care Unit, Department of Cardiology, Internal Medicine Clinic, Sestre Milosrdnice University Hospital Center, Zagreb, Croatia

⁶Department of Emergency Medicine, Internal Medicine Clinic, Sestre Milosrdnice University Hospital Center, Zagreb, Croatia

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Introduction

Central obesity is directly associated with insulin resistance, dyslipidemia and inflammation, which lead to atherosclerotic vascular disease [1]. There is a positive association of central obesity, as well as a negative association of overall obesity, with higher mortality in acute coronary syndrome, as body mass index (BMI) does not adequately discriminate the difference between body fat and lean muscle mass [2]. The newest obesity parameter, the relative fat mass index (RFMI), was more accurate for body fat-defined obesity and more accurate than BMI for those with a high body fat percentage [3].

Aim

We investigated the unknown interrelation between the RFMI and other obesity indices in predicting clinical severity and prognosis of acute ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI).

Material and methods

This prospective study, approved by the appropriate ethics committee, included 250 patients with acute STEMI treated with primary PCI. The inclusion criteria were: presenting within 12 h from the onset of symptoms (history of chest pain/discomfort lasting for 10–20 min or more, not responding fully to nitroglycerine), persistent ST-segment elevation on electrocardiography (ECG) in at least two consecutive leads or (presumed)

new left bundle branch block (LBBB), and elevated cardiac laboratory biomarkers (cardiac troponin T (cTnT) and creatine kinase (CK)). The diagnosis of acute STEMI was established and primary PCI performed using the European Society of Cardiology criteria [4, 5]. After primary PCI, patients were classified into two groups (with/without RFMI obesity) which were analyzed by baseline, as well as severity and prognostic parameters of acute STEMI.

Baseline demographic and medical history parameters included gender, age, hypertension, dyslipidemia, hyperglycemia, anthropometry, smoking, known family history of cardiovascular events (MI, stroke), previous MI, previous PCI and coronary artery bypass grafting (CABG). Anthropometric baseline data included BMI, waist circumference (WC), waist-to-hip (WHR) and waist-to-height ratio (WHtR). RFMI was calculated using the equation $RFMI = 64 - (20 \times \text{height/waist}) + (12 \times \text{sex})$, where sex = 0 for men and 1 for women [3]. Increased RFMI values were defined as $\geq 25\%$, $\geq 28\%$ and $\geq 30\%$ for males aged 20–39, 40–59 and 60–79 years, respectively. For females, increased RFMI values were defined as $\geq 39\%$, $\geq 40\%$ and $\geq 42\%$ for ages 20–39, 40–59 and 60–79 years, respectively.

The severity of acute STEMI included: clinical presentation (angina pectoris, dyspnea, and length of hospital stay), in-hospital complications (arrhythmias, heart failure, cardiogenic shock, cardiac arrest, mechanical ventilation, reinfarction, repeated PCI, mortality, and total in-hospital complications), coronary angiography, laboratory (creatinine clearance, maximal cTnT and CK) and

Corresponding author:

Marko Mornar Jelavic MD, PhD, Institute for Cardiovascular Prevention and Rehabilitation, Zagreb, Croatia, phone: +38 5(91)7826135, e-mail: mjelavic@yahoo.com

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echocardiography findings (left ventricular ejection fraction – LVEF).

Coronary angiography was performed by applying a monoplane system (Axiom Artis, Siemens, Erlangen, Germany) [5]. Patients received 70 IE/kg of unfractionated heparin, 300 mg of aspirin, a loading dose of 600 mg of clopidogrel, and a GPIIb/IIIa inhibitor according to the judgment of an interventional cardiologist. Stenosis of more than 50% was considered clinically significant. It was measured with the system software at all patients. We analyzed the number of significantly narrowed coronary arteries (CAs), their segments (proximal, middle and distal) [6], and the number, length and diameter of used stents.

Serum CK activity was measured by spectrophotometry (Olympus 680, Beckman Coulter Inc., California, USA), while cTnT levels were measured by electrochemiluminescence (ECL) assay (Cobas e411, Roche Diagnostics, Sussex, UK). During hospitalization, echocardiography was performed in all patients (Acuson Sequoia 512, Siemens, Munich, Germany) [7].

During hospitalization, 19 (7.6%) patients died and 231 (92.4%) entered 12-month prognostic evaluation with monitoring of major adverse cardiovascular events (MACE): cardiac (reinfarction, restenosis, new stenosis, urgent CABG, other (e.g. heart failure)) and non-cardiac rehospitalizations (stroke, other (e.g. peripheral artery disease)), and mortality. Data were collected by medical examination, checking medical documentation, or telephone contact with patients, family members or home physicians.

Statistical analysis

Qualitative data were presented in absolute number and percentage. We used the χ^2 test with Yates correction. Quantitative data were presented as median and range. Differences between the two groups were tested by Mann-Whitney *U* test. Correlations between the anthropometric parameters with clinical severity and prognosis were investigated by Spearman's correlation and classified as very weak (0–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79) and very strong (0.80–1.0). This guide also applies to negative correlations. We used Cox proportional-hazards regression for analyzing the effect of several risk factors on prognosis. The level of statistical significance was set at $p < 0.05$ (Statistica 6.0 for Windows).

Results

RFMI obese subjects (55.2%) had higher rates of arterial hypertension (80.4% vs. 67.0%) and dyslipidemia (81.2% vs. 69.6%), higher median values of BMI (29.4 vs. 25.6 kg/m²), WC (106 vs. 93 cm), WHR (1.0 vs. 0.9) and WHtR (0.62 vs. 0.53), higher rates of in-hospital complications (47.8% vs. 33.9%), and higher median diameter

of stents (3.5 vs. 3.0 mm) ($p < 0.05$), without significant differences between the two groups in other baseline parameters and parameters of clinical severity and prognosis.

We found a negative correlation of BMI with the significantly stenosed proximal CA segments and a positive correlation with stents diameter; positive correlations of WC with hospital stay and stents diameter; positive correlations of WHtR with hospital stay, in-hospital complications and stents diameter; a positive correlation of RFMI with in-hospital complications and negative correlations with parameters of myocardial necrosis (cTnT, CK) ($p < 0.05$) (Tables I and II).

After primary PCI, all patients were taking dual antiaggregation therapy and statins, while the most commonly prescribed drugs were angiotensin converting enzyme inhibitors (ACEIs)/angiotensin-receptor blockers (ARBs) (72.1%) and β -blockers (59.7%), then diuretics (13.9%) and calcium-channel blockers (CCB) (8.7%). There were no significant correlations between the anthropometric parameters and MACE. However, there were significant positive correlations between the number of significantly stenosed CAs and MACE ($\rho = 0.24$, 95% CI: 0.12–0.36), and the number of proximal and distal significantly stenosed CA segments and MACE ($\rho = 0.14$, 95% CI: 0.01–0.27 and $\rho = 0.19$, 95% CI: 0.06–0.31, respectively); and a negative correlation between the LVEF and MACE ($\rho = -0.15$, 95% CI: –0.27 to –0.02) ($p < 0.05$).

Cox analysis revealed no effect of several risk factors on MACE, i.e. of age (hazard ratio (HR) = 1.02, 95% CI: 0.99–1.05, $p = 0.060$), male gender (HR = 0.94, 95% CI: 0.50–1.78, $p = 0.848$), hypertension (HR = 1.57, 95% CI: 0.77–3.23, $p = 0.203$), dyslipidaemia (HR = 0.82, 95% CI: 0.44–1.55, $p = 0.555$), hyperglycemia (HR = 0.93, 95% CI: 0.52–1.66, $p = 0.801$), smoking (HR = 0.69, 95% CI: 0.39–1.23, $p = 0.208$), in-hospital complications (HR = 0.98, 95% CI: 0.55–1.77, $p = 0.949$), creatinine clearance (HR = 1.00, 95% CI: 0.99–1.02, $p = 0.225$), BMI (HR = 0.97, 95% CI: 0.91–1.04, $p = 0.974$), WC (HR = 1.00, 95% CI: 0.98–1.02, $p = 0.999$), WHR (HR = 1.90, 95% CI: 0.07–51.5, $p = 0.704$), WHtR (HR = 1.27, 95% CI: 0.03–50.6, $p = 0.898$) and RFMI (HR = 1.00, 95% CI: 0.97–1.05, $p = 0.745$), except LVEF (HR = 0.96, 95% CI: 0.94–0.99, $p = 0.034$) and significantly stenosed CAs (HR = 1.90, 95% CI: 1.35–2.62, $p < 0.001$). After adjustment of MACE with these two factors, we found the effect of significantly stenosed CAs on MACE (HR = 1.78, 95% CI: 1.26–2.52, $p = 0.001$).

Discussion

Studies have reported that overall obese patients have greater CA and stent diameters, normal LVEF, lower CK levels, lower in-hospital and overall mortalities, and lower rates of MACE during 12-month follow-up [8–10]. In this study, this overall “obesity paradox” could explain

Table I. Correlation between BMI, WC and clinical severity and prognosis of acute STEMI

Parameter	BMI (rho) (95% CI)	P-value	WC (rho) (95% CI)	P-value
Hospital stay [days]	0.07 (–0.06 to 0.20)	0.271	0.14 (0.02–0.27)	0.025
Clinical presentation	–0.06 (–0.18 to 0.06)	0.331	–0.00 (–0.13 to 0.12)	0.978
In-hospital complications	0.00 (–0.12 to 0.12)	0.998	0.07 (–0.05 to 0.19)	0.265
Maximal cTnT [ng/ml]	–0.11 (–0.23 to 0.19)	0.098	–0.04 (–0.17 to 0.08)	0.503
Maximal CK [U/l]	–0.04 (–0.17 to 0.08)	0.515	–0.02 (–0.15 to 0.10)	0.744
LVEF (%)	0.01 (–0.12 to 0.14)	0.840	0.04 (–0.09 to 0.17)	0.537
Proximal CA segments	–0.15 (–0.27 to –0.02)	0.019	–0.04 (–0.17 to 0.08)	0.508
Distal CA segments	–0.11 (–0.24 to 0.01)	0.073	–0.08 (–0.20 to 0.04)	0.205
Stents	–0.07 (–0.19 to 0.06)	0.320	–0.12 (–0.25 to 0.01)	0.063
Diameter of stents [mm]	0.24 (0.12–0.36)	< 0.001	0.15 (0.03–0.28)	0.019
Length of stents [mm]	0.06 (–0.07 to 0.19)	0.381	0.12 (–0.01 to 0.24)	0.081
Total MACE	–0.03 (–0.16 to 0.09)	0.624	–0.00 (–0.13 to 0.13)	0.996

BMI – body mass index, CAs – coronary arteries, CI – confidence interval, CK – creatine kinase, cTnT – cardiac troponin T, LVEF – left ventricle ejection fraction, MACE – major adverse cardiovascular events, RFMI – relative fat mass index, STEMI – ST-elevation myocardial infarction, WC – waist circumference. Statistical significance defined as $p < 0.05$.

Table II. Correlation between WHR, WHtR, RFMI and clinical severity and prognosis of acute STEMI

Parameter	WHR (rho) (95% CI)	P-value	WHtR (rho) (95% CI)	P-value	RFMI (rho) (95% CI)	P-value
Hospital stay [days]	0.04 (–0.09 to 0.17)	0.543	0.14 (0.02–0.26)	0.028	0.12 (–0.00 to 0.25)	0.058
Clinical presentation	–0.04 (–0.17 to 0.08)	0.495	–0.02 (–0.15 to 0.10)	0.716	0.04 (–0.08 to 0.17)	0.505
In-hospital complications	–0.06 (–0.18 to 0.06)	0.346	0.12 (0.00–0.24)	0.049	0.16 (0.04–0.28)	0.010
Maximal cTnT [ng/ml]	–0.03 (–0.15 to 0.10)	0.687	–0.10 (–0.22 to 0.03)	0.119	–0.18 (–0.29 to –0.06)	0.006
Maximal CK [U/l]	–0.00 (–0.13 to 0.12)	0.977	–0.08 (–0.20 to 0.05)	0.210	–0.17 (–0.28 to –0.05)	0.010
LVEF (%)	0.07 (–0.06 to 0.20)	0.285	0.05 (–0.08 to 0.17)	0.469	0.06 (–0.07 to 0.19)	0.377
Proximal CA segments	–0.00 (–0.13 to 0.12)	0.950	–0.00 (–0.13 to 0.12)	0.973	0.01 (–0.12 to 0.13)	0.925
Distal CA segments	–0.08 (–0.20 to 0.05)	0.236	–0.05 (–0.18 to 0.07)	0.389	0.04 (–0.08 to 0.17)	0.492
Stents	–0.04 (–0.17 to 0.09)	0.553	–0.09 (–0.22 to 0.04)	0.156	–0.12 (–0.24 to 0.01)	0.081
Diameter of stents [mm]	0.08 (–0.05 to 0.21)	0.226	0.14 (0.01–0.27)	0.031	0.03 (–0.10 to 0.15)	0.696
Length of stents [mm]	0.05 (–0.08 to 0.18)	0.447	0.08 (–0.05 to 0.21)	0.223	–0.01 (–0.14 to 0.12)	0.859
Total MACE	0.03 (–0.10 to 0.16)	0.662	0.01 (–0.12 to 0.14)	0.936	0.04 (–0.09 to 0.16)	0.591

CAs – coronary arteries, CK – creatine kinase, cTnT – cardiac troponin T, LVEF – left ventricle ejection fraction, MACE – major adverse cardiovascular events, RFMI – relative fat mass index, STEMI – ST-elevation myocardial infarction, WHR – waist to hip ratio, WHtR – waist to height ratio. Statistical significance defined as $p < 0.05$.

the lack of significant correlation between the values of BMI and clinical severity and prognosis, as well as the significant negative correlation of BMI with the number of significantly stenosed proximal CA segments.

Increased WC is associated with greater myocardial necrosis and worse LVEF in acute MI [11, 12]. We found the central “obesity paradox”, with no significant correlation between the values of WC and clinical severity and prognosis, except a positive significant correlation of WC with hospital duration and stent diameter.

Patients with acute STEMI and increased WHR more frequently have heart failure; WHR is an independent predictor of 6-month mortality [13]. Our study revealed another example of the central “obesity paradox”, with no significant correlation between the values of WHR and clinical severity and prognosis.

Among the obesity indices, WHtR has the strongest positive correlation with CAD [14]. Our values of WHtR positively correlated with hospital stay, in-hospital complications, and diameter of stents.

Other authors reported that the RFMI was more accurate than BMI to estimate whole-body fat percentage and improved body fat-defined obesity misclassification among American adult individuals of Mexican, European or African ethnicity [3]. In this study, the values of RFMI positively correlated with in-hospital complications and negatively with laboratory parameters of myocardial necrosis (cTnT, CK).

Finally, the number of significantly stenosed CAs positively correlated with MACE, which is consistent with the literature data [15].

Conclusions

RFMI and WHtR are superior in predicting clinical severity (hospital stay, in-hospital complications) of acute STEMI, while none of the obesity indices have a role in predicting prognosis. We propose more frequent use of RFMI and WHtR in everyday clinical work in patients suffering from myocardial infarction.

Conflict of interest

The authors declare no conflict of interest.

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