Metabolic Syndrome is Associated With Higher Wall Motion Score and Larger Infarct Size After Acute Myocardial Infarction

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Background: Infarct size is an important surrogate end point for early and late mortality after acute myocardial infarction. Despite the high prevalence of metabolic syndrome in patients with atherosclerotic diseases, adequate data are still lacking regarding the extent of myocardial necrosis after acute myocardial infarction in these patients.

Objectives: In the present study we aimed to compare myocardial infarction size in patients with metabolic syndrome to those without metabolic syndrome using peak CK-MB and cardiac troponin I (cTnI) at 72 hours after the onset of symptoms.

Patients and Methods: One-hundred patients with metabolic syndrome (group I) and 100 control subjects without metabolic syndrome (group II) who experienced acute myocardial infarction were included in the study. Diagnosis of metabolic syndrome was based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines published in 2001. Myocardial infarction size was compared between the two groups of patients using peak CK-MB and cTnI level in 72 hours after the onset of symptoms.

Results: Peak CK-MB and cTnI in 72 hours were found to be significantly higher in patients with metabolic syndrome compared with control subjects (both P < 0.001). Patients with metabolic syndrome also had markedly higher wall motion abnormality at 72 hours after the onset of symptoms as assessed by echocardiographically-derived Wall Motion Score Index (WMSI) (P < 0.001). Moreover, statistically significant relationships were found between WMSI and peak CK-MB and also cTnI at 72 hours (Spearman's rho = 0.56, P < 0.001 and Spearman's rho = 0.5, P < 0.001; respectively). However, association between WMSI and left ventricular ejection fraction was insignificant (Spearman's rho = -0.05, P = 0.46).

Conclusions: We showed that patients with metabolic syndrome have larger infarct size compared to control subjects.

Keywords: Creatine Kinase; Echocardiography; Myocardial infarction; Troponin

1. Background

The metabolic syndrome (also named insulin resistance syndrome or syndrome X) is defined as the clustering of interrelated atherosclerotic risk factors including insulin resistance, high blood pressure, a low level of high-density lipoprotein (HDL) cholesterol, a high triglyceride level, a high plasma glucose concentration, and central obesity (1-3). Coronary artery disease and stroke have been reported to be three-times higher in patients with the metabolic syndrome compared with those without metabolic syndrome (4). The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines published in 2001 introduced the metabolic syndrome as a new target for cardiovascular risk reduction therapy beyond low-density lipoprotein (LDL) cholesterol lowering (5).

Following acute myocardial infarction, prognosis is largely related to the extent of myocardial necrosis and the resultant decline in left ventricular function (6). Infarct size is an important surrogate end point for early and late mortality after acute myocardial infarction (AMI) (7). Several methods have been used to estimate infarct size in patients with AMI including global left ventricular function or ejection fraction, end systolic volume, regional wall motion, creatine kinase release, thallium infarct size, QRS score based on evolutionary ST and T wave changes, radionuclide myocardial perfusion imaging with 99 m-technetium sestamibi and late gadolinium-enhanced cardiovascular magnetic resonance (CMR). Accumulating evidence has consistently confirmed the usefulness of cTnT or cTnI for the estimation of infarct size (8-10).

Despite the high prevalence of metabolic syndrome in patients with atherosclerotic diseases and also considerable morbidity and mortality of acute coronary syn-

dromes in patients with metabolic syndrome, adequate data are still lacking regarding the extent of myocardial necrosis after AMI in patients with metabolic syndrome.

2. Objectives

In the present study we aimed to evaluate myocardial infarction size, as estimated by means of cardiac enzymes and echocardiographically-derived wall motion score index (WMSI) in patients with metabolic syndrome comparing to control individuals.

3. Patients and Methods

3.1. Study Population

The study group consisted of a consecutive series of 200 patients with first acute myocardial infarction (AMI) admitted to the coronary care unit at Rajaei Cardiovascular, Medical and Research Center (Tehran, Iran) from April 2011 to June 2013. Patients were included if they met the universal definition of acute myocardial infarction (11) and had no history of documented prior coronary artery disease, AMI, coronary bypass surgery, valvular heart disease, left ventricular dysfunction, left ventricular hypertrophy, atrial fibrillation, uncontrolled hypertension or poorly controlled obstructive airway disease.

Patients were eligible whether presenting with ST-segment elevation myocardial infarction (STEMI) or non–ST-segment elevation myocardial infarction (NSTEMI). Patients who underwent percutaneous coronary intervention as part of reperfusion therapy (those patients with STEMI presenting within 12 hours of onset of symptoms) and also those with recurrent AMI or congestive heart failure during hospital admission were excluded. For patients presenting with NSTEMI, initial antithrombotic therapy was instituted and subsequent angiography was performed within the first week after the required data were obtained for the study.

Eligible patients were classified according to the National Cholesterol Education Program Adult Treatment Panel III guideline into the 2 groups of patients with and without metabolic syndrome.

3.2. Diagnostic Criteria for Metabolic Syndrome

The diagnosis of metabolic syndrome was based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines published in 2001 (5). According to this guideline, patients were found to have metabolic syndrome when three or more of the following criteria were present: 1) abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women); 2) a high triglyceride level (> 150 mg/dL); 3) a low HDL-cholesterol level (< 40 mg/dL in men and < 50 mg/dL in women); 4) high blood pressure (systolic > 130 mmHg or diastolic > 85 mmHg, or on antihypertensive medication); and 5) a high fasting plasma glucose concentration

(> 110 mg/dL). Control subjects had only ≤ 2 of these components.

3.3. Cardiac Enzymes Assay

Serum cardiac troponin I (cTnI) level at 72 hours after presentation of acute myocardial infarction (from symptom-onset) and peak creatine kinase-MB fraction (CK-MB) level were used for estimation of infarct size. Serum CK-MB was measured with 12-hour intervals during the first 5 days after symptom-onset and the peak level was used for this purpose.

3.4. Biochemical Analysis

Blood samples were taken after a 12-hours fasting from an antecubital vein with a 19-gauge needle without venous stasis for measuring total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, and fasting plasma glucose levels approximately 7-10 days after hospitalization for recent acute myocardial infarction. Plasma was immediately obtained by centrifugation of the blood at 3000 g for 15 minutes. Serum concentrations of total cholesterol and triglycerides were measured by fully enzymatic techniques. HDL-cholesterol was determined after precipitation of apolipoprotein B–containing lipoproteins with chloride and dextran sulfate. LDL-cholesterol was calculated as described by Friedewald et al. (12). Plasma glucose was measured with the glucose oxidase technique.

3.5. Anthropometric Measurements

Height, weight, and waist circumference were measured according to a standardized protocol. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m^2). The waist circumference was measured at its smallest point with the abdomen relaxed.

3.6. Standard Echocardiography

Transthoracic echocardiography was performed at a median five days [IQR 2 to 9 days] after AMI using a commercially available ultrasound system (Vivid 7, GE Medical Systems, Inc., Horten, Norway). All images were analyzed offline by a single investigator, blinded to all clinical data. Images were acquired at the end of expiration with the subjects at rest, lying in the left lateral decubitus position. Two-dimensional ECG was superimposed on the images, and end-diastole was considered at the peak R wave of the ECG. Standard two-dimensional measurements and pulsed-wave Doppler echocardiography were performed. Left ventricular ejection fraction (LVEF) was calculated using the modified biplane Simpson method as recommended by the American of Echocardiography. Measurements were averaged over at least three cardiac cycles. Regional wall motion was evaluated using a 16-segment model as recommended by the European Societ-

ies of Echocardiography (13). The left ventricle (LV) was divided into six basal segments (anterior, anterolateral, inferolateral, inferior, inferoseptal, and anteroseptal), six middle segments (same subgroups), and four apically located segments (anterior, septal, inferior, and posterior). By visual analysis of systolic wall thickening, segments were assigned a wall motion score (WMS) as follows: 1, normal or hyperkinetic (normal endocardial excursion and systolic wall thickening); 2, hypokinetic (reduced excursion and wall thickening); 3, akinetic (absent excursion and wall thickening); and 4, dyskinetic (paradoxical systolic outward wall motion). WMS index (WMSI) was calculated by dividing the sum of all WMS by the total number of segments analyzed. For estimation of WMSI, the intraclass correlation coefficients for intraobserver and interobserver reproducibility were 0.95 (0.78 to 0.98) and 0.89 (0.76 to 0.98), respectively.

3.7. Statistical Analysis

All analyses were conducted by statistical package for social sciences (SPSS) software, version 19 (SPSS Inc., Chicago, IL, USA). All data initially were analyzed using the Kolmogorov-Smirnov test to assess for normality. Continuous data are presented as mean ± SD when normally distributed and median with interquartile range (IQR) when non-Gaussian in distribution. Unpaired t-tests and Mann-Whitney-U rank sum tests were used for bivariate analyses of normally and non-normally distributed continuous data, respectively. Categorical data were given as frequencies and percentages, and bivariate analyses of these data were performed using chi-square or Fisher's exact tests, when appropriate. The correlations between echocardiographic measures and cardiac enzymes were assessed by the spearman correlation test. A P value of < 0.05 was considered statistically significant. A multiple regression analysis was performed to further quantify

the relationships between regional wall mostion score index (RWMSI), and cardiac enzymes and also the components of the metabolic syndrome. The median RWMSI was regressed for waist circumference, BMI, HDL-cholesterol, LDL-cholesterol, total cholesterol, fasting plasma glucose, triglyceride level, systolic and diastolic blood pressure, peak CK-MB and cTnI at 72 hours.

4. Results

Baseline characteristics of patients with metabolic syndrome and controls are presented in Table 1. Patients with metabolic syndrome were older, and had higher diastolic blood pressure, BMI, waist circumference, serum triglyceride, total cholesterol, LDL-cholesterol and fasting plasma glucose and lower HDL-cholesterol compared with control subjects. However, no significant differences were seen between the two groups with respect to gender, systolic blood pressure and the status of cigarette smoking. The relative frequency of each component of the metabolic syndrome is shown in Table 2. An increased blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg) and a high triglyceride level (> 150 mg/dL) were the most frequent components of the metabolic syndrome in the metabolic syndrome group (96% and 90%, respectively). In patients with metabolic syndrome, three, four and five components of the metabolic syndrome were found to be present in 16 (16%), 46 (46%), and 38 (38%) patients, respectively.

The distribution of various types of ST-elevation myocardial infarction as well as NSTEMI in patients with and without metabolic syndrome is depicted in Figure 1. Patients with metabolic syndrome were more likely to have anterior or anterolateral ST-segment elevation myocardial infarction (STEMI) while inferior and inferoposterior STEMI were more prevalent in patients without metabolic syndrome (P = 0.003).

Table 1. Baseline Characteristics of Study Population [a]

Variable	Metabolic Syndrome (+)	Metabolic Syndrome (-)	P Value
Age, yr	63 (62-72)	62 (58-68)	0.001
Gender, %			0.082
Male	78 (78)	67 (67)	
Female	22 (22)	33 (33)	
Current smoking	42 (42)	39 (39)	0.076
Body mass index, kg/m^2	31.34 ± 3.91	29.66 ± 3.55	0.005
Waist circumference, cm	105 (99-109)	84 (78-88)	< 0.001
Systolic blood pressure, mmHg	134.37 ± 23.88	133.53 ± 23.98	0.940
Diastolic blood pressure, mmHg	87.40 ± 3.07	79.44 ± 9.89	< 0.001
Fasting blood glucose, mg/dL	143 (124-163)	82 (72-116)	< 0.001
Triglyceride, mg/dL	186 (175-198)	179 (140-185)	< 0.001
Total cholesterol, mg/dL	201 (187-243)	198 (181-213)	0.041
LDL-cholesterol, mg/dL	184 (131-245)	136 (97-163)	< 0.001
HDL-cholesterol, mg/dL	34 (25-43)	42 (31-46)	< 0.001
Number of components of metabolic syndrome	1.03 ± 0.27	4.28 ± 0.65	0.001

[a] Mean ± SD or median (interquartile range).

Table 2. Relative Frequency of Each Component of Metabolic Syndrome in Metabolic Syndrome Group

Variable	No. (%)
Abdominal obesity (waist circumference)	65 (65)
> 88 cm in women	
> 102 cm in men	
Blood pressure, mmHg	96 (96)
Systolic ≥ 130	
Diastolic ≥ 85	
High fasting plasma glucose, mg/dL (≥ 110)	74 (74)
High triglyceride level, mg/dL (≥ 150)	90 (90)
Low HDL-cholesterol level, mg/dL	68 (68)
< 50 for women	
< 40 for men	

In Table 3, a comparison of echocardiographic measures has been made between the patients with metabolic syndrome and control subjects. As shown, except for tricuspid regurgitation gradient (TRG), no significant differences were seen between the two study groups with respect to conventional echocardiographic parameters. However, severity of diastolic dysfunction was significantly higher in patients with metabolic syndrome as compared to control subjects (Table 3, P = 0.002). Transmitral Doppler echocardiography also showed higher E wave and A wave velocities in patients with metabolic syndrome than in controls (Table 4, p=0.003 and 0.012, respectively).

4.1. Estimation of the Infarct Size by Cardiac Enzymes

Peak CK-MB was significantly higher in patients with metabolic syndrome as compared to control subjects (median: 390 ng/mL, IQR: 379-410 ng/mL versus median: 287 ng/mL, IQR: 275-296 ng/mL; P < 0.001). Patients with

Table 3. Conventional Echocardiographic Characteristics [a]

Parameter	Metabolic Syndrome (+)	Metabolic Syndrome (-)	P Value
PWT, cm	0.97 ± 0.11	0.93 ± 0.15	0.298
IVST, cm	0.96 ± 0.10	0.93 ± 0.11	0.237
LVEDD, cm	4.50 ± 0.53	4.38 ± 0.53	0.311
LVESD, cm	2.97 ± 0.64	2.78 ± 0.45	0.326
LVEF, %	58.13 ± 9.71	58.72 ± 5.60	0.967
WMSI	2.91 (2.54-3.29)	2.29 (2.11-2.41)	< 0.001
PAP, mmHg	34.44 ± 8.81	30.16 ± 5.98	0.662
TRG, mmHg	27.69 ± 7.86	23.65 ± 5.77	0.039
TAPSE, mm	17.35 ± 3.75	17.06 ± 3.96	0.795
Pericardial effusion			0.087
Small	6 (6)	7 (7)	
Moderate	3 (6)	1 (1)	
Large	1 (6)	1 (1)	
Mitral regurgitation			0.065
Trivial	5 (5)	6 (6)	
Mild	13 (13)	16 (16)	
Mild to moderate	4 (4)	4 (4)	
Moderate	2 (2)	4 (4)	
Moderate to severe	3 (3)	6 (6)	
Severe	4 (4)	3 (3)	
Severity of diastolic dysfunction			0.002
Mild	8 (8)	5 (5)	
Moderate	5 (5)	3 (3)	
Severe	8 (8)	7 (7)	

[a] Data are presented as No. (%) or Mean ± SD and median (interquartile range).ظ

Table 4. Transmitral Doppler Data

	Metabolic Syndrome (+)	Metabolic Syndrome (-)	P Value
Peak early diastolic velocity (E), m/s	0.85 ± 0.13	0.80 ± 0.19	0.003
Peak late diastolic velocity (A), m/s	1.88 ± 0.45	1.81 ± 0.53	0.012

metabolic syndrome also had higher cTnI level at 72 hours after the onset of symptoms comparing to controls (median: 18 μg/L, IQR: 17-19 μg/L versus median: 12 μg/L, IQR: 11-13 μg/L; P < 0.001).

4.2. Estimation of the Infarct Size by Echocardiography

Median regional wall motion score index was 2.91 (IQR: 2.54-3.29) in patients with metabolic syndrome, which was markedly higher than in control patients (median: 2.29, IQR: 2.11-2.41; P < 0.001). No significant correlation was found between RWMSI and left ventricular ejection fraction (Spearman's rho = -0.05, P = 0.46). This correlation was also insignificant in both groups of patients with and without metabolic syndrome (P = 0.47 and P = 0.32, respectively). However, RWMSI and peak CK-MB were positively correlated (Spearman's rho = 0.56, P < 0.001, Figure 2). Higher RWMSI was also significantly associated with an increased cTnI serum level at day 3 (Spearman's rho = 0.50, P < 0.001, Figure 3).

Figure 1. The Distribution of Various Types of Acute Myocardial Infarction in Patients With and Without Metabolic Syndrome (P = 0.003)
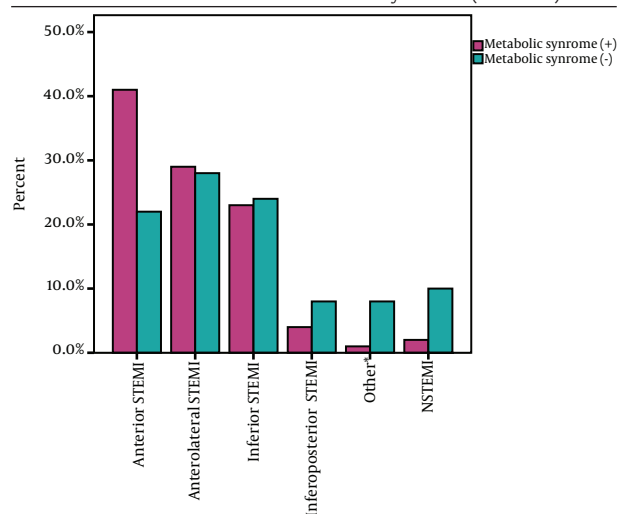
* Other: infarction involving either right ventricle or interventricular septum.
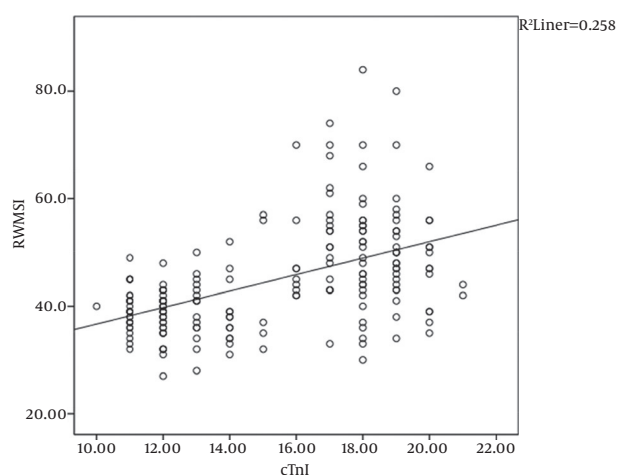

Figure 2. Peak CK-MB Level and RWMSI are Positively Correlated (Spearman's rho = 0.56, P < 0.001) in Patients With Acute ST Elevation Myocardial Infarction

Figure 3. Cardiac Troponin I Level at 72 Hours After Onset of Symptoms and RWMSI Are Positively Correlated (Spearman's rho = 0.50, P < 0.001) in Patients With Acute Myocardial Infarction

Table 5. Estimation of Infarct Size in Various Types of AMI [a, b]

Type of AMI	Anterior STEMI	Anterolateral STEMI	Inferior STEMI	Inferoposterior STEMI	Other [c]	NSTEMI	P Value
CK.MB, mg/dL	367.5 (296.75-395.50)	350 (290-397)	300.00 (283-390)	296.50 (291.5-382.5)	277.00 (245-299.5)	289 (279.25-298.75)	0.005
cTnI, mg/dL	17 (13-19)	16 (12-18)	15 (12-19)	12.5 (11-17.75)	12 (11.5-12.5)	12 (11-14)	0.002
LVEF, %	35 (30-40)	35 (32.5-40)	35 (30-40)	35 (30-40)	40 (35-42.5)	35 (30-40)	0.57
WMSI	2.58 (2.23-2.94)	2.64 (2.17-3.17)	2.41 (2.17-2.94)	2.35 (2.23-2.75)	2.41 (2.29-2.55)	2.38 (2.29-2.45)	0.35

[b] other: infarctions involving either right ventricle of interventricular septum.
[a] Data are presented as median (interquartile range).
[b] Abbreviations: AMI, acute myocardial infarction; CK-MB, creatine kinase-MB fraction; cTnI, cardiac troponin I; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; WMSI, wall motion score index.
[c] Other: ST-segment elevation myocardial infarctions involving either right ventricle of interventricular septum.

Peak CK-MB level and cTnI level at 72 hours were significantly different in various types of acute myocardial infarction (P = 0.005 and 0.002; respectively, Table 5). However, LVEF and WMSI were statistically similar in all types of acute myocardial infarction (P = 0.57 and 0.35; respectively, Table 5).

No statistically significant correlations were also seen between left ventricular ejection fraction and either peak CK-MB or cTnI at 72 hours (Spearman's rho = -0.055, P = 0.051 and Spearman's rho = -0.059, P = 0.052; respectively).

The results of multiple regression analysis indicated statistically significant relationships between median RWMSI and waist circumference (P < 0.001), LDL-cholesterol level (P = 0.005) and peak CK-MB (P = 0.014).

5. Discussion

The main finding of this study is that patients with metabolic syndrome have significantly higher infarct size compared to those without metabolic syndrome.

A growing body of literature has been shown that metabolic syndrome, as defined by the NCEP ATP III criteria, is very common among patients with symptomatic arterial disease, and is also associated with advanced vascular damage and subsequently worse prognosis (14).

Metabolic syndrome represents a collection of several cardiovascular risk factors, each of which may play an important role in this poor outcome. In a large study on 1108 patients with symptomatic coronary artery disease, metabolic syndrome has been found in 51% of the patients (15). The results of this study also demonstrated that the number of components of metabolic syndrome, as defined by the NCEP ATP III criteria, increases with the severity of angiographically-proven coronary artery disease.

Moreover, it has been demonstrated that increased number of components of the metabolic syndrome was associated with a higher mean carotid intima media thickness and also a lower ankle brachial pressure index in patients with coronary heart disease, peripheral arterial disease, or abdominal aortic aneurysm (14). Patients with metabolic syndrome, which had angiographically-proven normal coronary arteries, have been shown to have significantly higher thrombolysis in myocardial infarction (TIMI) frame count for all three major epicardial coronary vessels, compared to those without metabolic syndrome (16).

In addition, impacts of metabolic syndrome on outcome of patients with myocardial infarction have been shown previously. Patients with metabolic syndrome have been shown to have higher case fatality rate following acute myocardial infarction (17). In a large study involving 4483 patients aged 35 to 70 years in Finland and Sweden, metabolic syndrome -as defined by the World Health Organization- was present in approximately 80% of subjects with type two diabetes mellitus (DM) (18). In that study, individuals with metabolic syndrome had markedly higher cardiovascular case fatality rate compared to individuals without metabolic syndrome (12.0% versus 2.2%; P < 0.001). In a population-based registry of patients with myocardial infarction, metabolic syndrome - as defined by the NCEP ATP III criteria - has been demonstrated to be associated with worse in-hospital outcome (17). The results of that study also revealed that patients with metabolic syndrome are at increased risk of development of heart failure and cardiogenic shock as compared to patients without metabolic syndrome. They also found that among all components of metabolic syndrome, hyperglycemia seems to be the major determinant of this increased risk of heart failure.

Logstrup et al. in an observational study assessed the effects of known DM, newly diagnosed DM, and impaired glucose tolerance (IGT) on echocardiography-derived coronary flow reserve (CFR) in a group of patients with recent AMI (19). They found persistent association between a decreased CFR and overt or newly diagnosed DM but not the IGT. They demonstrated that CFR in patients with IGT was not different from CFR in patients with normal glucose metabolism.

Fujimoto et al. demonstrated that hyperglycemia is associated with suppressed coronary microcirculation in healthy young adults (20). The leukocyte capillary plugging, enhanced shear stress-induced platelet activation, and accumulation of advanced glycation products (21, 22) result from persistent hyperglycemia and have been considered as probable mechanisms, which might explain the association between hyperglycemia and microvascular dysfunction.

However, very limited clinical data have addressed myocardial infarction size in patients with metabolic syndrome comparing to control subjects without metabolic syndrome. According to results of the present study, patients with metabolic syndrome had larger infarct size than control subjects. This finding might partly explain the higher risk of development of heart failure following acute myocardial infarction in patients with metabolic syndrome. Notably, large observational studies have found heart failure as a major determinant of outcome after acute coronary syndromes (23-25). Moreover, it has been shown that increased incidence of congestive heart failure due to severe pump failure results in the higher in-hospital case fatality rate in diabetic patients as compared to patients without diabetes (26).

After acute myocardial infarction, the extent of myocardial damage determines the prognosis of patients to a large degree (6). In clinical practice, several non-invasive techniques are used to estimate infarct size and LV function including radionuclide imaging, technetium-99 m sestamibi or thallium scintigraphy. However, most of these modalities lack the adequate resolution or acceptable availability and cost-effectiveness (27). Among these techniques, late gadolinium-enhanced cardiovascular magnetic resonance has been found to have superior performance in the estimation of infarct size and quantification of LV function (28). Cardiac biomarkers

such as CK-MB and different types of cardiac troponins have gained increasing utility due to their ability in the diagnosis, stratification and also prediction of patients' outcome following acute coronary syndromes (29-31). There is convincing evidence from several trials that CK-MB and cardiac troponins I and/or T are also useful for rough estimation of the extent of myocardial damage (8-10, 32-34). The major limitation of cytoplasmic enzymes such as CK or CK-MB in the estimation of infarct size is the need for serial measurements to identify peak or cumulative serum concentrations. Furthermore, cytoplasmic enzymes are highly affected by reperfusion and also lack cardio-specificity (35). In contrast, cardiac troponins are cardiac-specific proteins that are incorporated in the contractile apparatus of cardiomyocytes. Except for the small cytosolic fraction, release of troponins after AMI is prolonged and is not influenced by the reperfusion of the infarct zone (35). Several experimental (36, 37) and clinical studies (38) have shown that a single cTnT-measured 72–96 hours after the onset of symptoms-is useful for estimation of infarct size and is at least as effective as several measurements of cardiac enzymes for assessment of cumulative release or peak values. Steen et al. in a study on 44 patients with first ST- and non-ST-segment elevation myocardial infarction showed that a single cTnT value at 72–96 hours after onset of symptoms can be reliably used for the estimation of left ventricular function and infarct size after acute myocardial infarction (39). In a trial in 65 patients, peak levels of CK-MB and troponin T have been shown to be correlated with SPECT infarct size and LV function on day three and three months after infarction (8). In another study on 23 patients with ST-elevation and 21 patients with non–ST-elevation myocardial infarction, peak level of troponin T at 96 hours was correlated with magnetic resonance imaging infarct size (40). In addition, infarct size as determined by peak serum concentration of creatine kinase or creatine kinase-MB or their area under the curve has been shown to be associated with worse outcome, including cardiogenic shock (41) congestive heart failure (42, 43) and short- and long-term mortality (44-47). In the present investigation, we used peak CK-MB and cardiac troponin I at 72 hours after the onset of symptoms to estimate size of myocardial infarction. We showed that patients with metabolic syndrome had higher serum levels of peak CK-MB and cTnI at 72 hours after symptoms onset comparing to those without metabolic syndrome. We also investigated echocardiographically-derived regional wall motion score index to give a rough estimate of myocardial infarction size. We demonstrate that patients with metabolic syndrome have significantly higher WMSI than control subjects. However, still there is a large discrepancy in the medical literature regarding the association between metabolic syndrome and infarct size. Clavijo et al. in a comparison between 167 non-diabetic patients with metabolic syndrome and 133 control patients without metabolic syndrome or diabetes mellitus demonstrated larger infarct size and higher

in-hospital complications in patients with metabolic syndrome (48). In another study, Kranjcec et al. in a study on 141 patients with metabolic syndrome and 89 control patients presenting with acute coronary syndrome, also showed that patients with metabolic syndrome had larger infarct size (49). Similar to our study, these two studies have used peak CK-MB to determine the infarct size (48, 49). On the other hand, Bohmer et al. in a cross-sectional study including 152 patients (33 patients with metabolic syndrome) found no significant difference in median infarct size, as assessed by late gadolinium enhanced magnetic resonance imaging, between patients with and without metabolic syndrome (50).

However, it is worth noting that RWMSI may not accurately reflect the myocardial infarct size as it is affected by several important limitations. First, regional wall motion abnormality in patients with acute myocardial infarction may not completely result from the current ischemia. In other words, previous ischemia or infarction could also decrease RWMSI. On the other hand, a temporarily reduced motion can be seen in hibernating or stunned myocardium following acute myocardial infarction, while these segments are not truly infarcted and would retain their function by time. Moreover, myocardial diseases such as myocarditis or cardiomyopathy could also reduce myocardial motion. Diastolic dysfunction is also able to affect RWMSI. However, we found a close relation between peak CK-MB and RWMSI. Moreover, cTnI level at 72 hours after the onset of symptoms was also positively correlated with RWMSI. In addition, on multiple regression analysis, waist circumference, LDL-cholesterol level and peak CK-MB level were independently correlated with RWMSI.

Diastolic dysfunction has been suggested as an important predictor of morbidity and mortality in patients with metabolic syndrome (51). Our investigation demonstrated that the presence and the severity of diastolic dysfunction are significantly higher in patients with metabolic syndrome as compared to control subjects without metabolic syndrome. This finding is consistent with those of prior study by Penjaskovic et al. which demonstrated that metabolic syndrome is associated with the presence of diastolic dysfunction (51). They also have found that the grade of diastolic dysfunction dependents on the number of components of metabolic syndrome. Moreover, Khan et al. showed a positive association between each component of metabolic syndrome and the grade of diastolic dysfunction (52).

In the present study, we also assessed the association of CK-MB, cTnI level at 72 hours and RWMSI with left ventricular systolic function. Our results showed that neither CK-MB nor cTnI were significantly correlated with left ventricular ejection fraction in both group of patients with and without metabolic syndrome. Though, considering the borderline p values, this lack-of-association between cardiac biomarkers and left ventricular systolic function might be explained by the relatively small sample size

in the current study. Moreover, Pride et al. showed that only in patients with moderate to large infarcts (infarct size of > 15%), left ventricular ejection fraction and infarct size are negatively correlated and every 5% increase in infarct size is associated with 6.1% decrease in LVEF (34). We also found that the association between echocardiographically-derived RWMSI and left ventricular ejection fraction was inconspicuous. However, Lebeau et al. in a study on 122 patients referred for evaluation of heart disease showed that WMSI and LVEF are in good correlation, when assessed by cardiac MRI (53).

There are some limitations in this study. Our sample size is relatively small and all participants were recruited from a single center rendering our study to selection bias. Moreover, our results would have higher reliability if we were able to use imaging modalities, which have been proven to estimate infarct size more accurately than cardiac enzymes assays or wall motion score index; such as late gadolinium-enhanced CMR.

In conclusion, the results of the present investigation suggest that patients with metabolic syndrome have higher infarct size than control subjects, as assessed by peak CK-MB and cTnI at 72 hours after the onset of symptoms. However, larger studies using more accurate diagnostic modalities for estimation of infarct size are required to confirm these findings.

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Authors' Contributions

Shokoufeh Hajsadeghi has contributed in study concept and design, critical revision and approval of the manuscript. Majid Haghjoo, Nima Babaali, Zahra Norouzzadeh and Maryam Mohsenian have contributed in study concept and design, data collection, critical revision, approval of the manuscript. Mitra Chitsazan and Mandana Chitsazan have contributed in study concept and design, analysis and interpretation, statistics, drafting, critical revision and approval of the manuscript.

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