Acta Biomed 2015; Vol. 86, N. 1: 86-91

Original article

Detrimental predictive effect of metabolic syndrome on postoperative complications in patients who undergoing coronary artery bypass grafting

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Summary. *Background:* The present study came to address the value of metabolic syndrome (MetS) in predicting postoperative outcome following coronary artery bypass grafting (CABG). *Methods:* In a retrospective study, a consecutive series of patients including 2010 subjects who underwent isolated CABG were reviewed. Baseline information and intraoperative details were collected by reviewing hospital-recorded files. The composite outcome of major adverse cardiac and cerebrovascular events (postoperative morbidity) was generated from the occurrence of myocardial infarction, cardiac arrhythmias, stroke, renal failure, and other cardiac-related problems. *Results:* Overall, 2010 patients who underwent isolated CABG were studied that among them 24.7% suffered from MetS. No difference was found in the prevalence of postoperative arrhythmias, brain stroke, multi-organ failure, and dialysis between the two groups with and without MetS. Early morbidity rate was 27.4% in MetS group and 27.8% in non-MetS group with no significant discrepancy. Using multivariable logistic regression modeling, we showed that MetS status could not predict postoperative morbidity; however, advanced age, history of congestive heart failure, higher Canadian Cardiovascular Society (CCS) scale, and longer cross-clamp time were main indicators of postoperative morbidity. *Conclusion:* MetS has no detrimental predictive effect on early postoperative morbidity in CABG patients. (www.actabiomedica.it)

Key words: metabolic syndrome, coronary artery bypass, morbidity, prediction

Introduction

The overall prevalence of metabolic syndrome (MetS) considerably varies among different ethnic groups and elevates markedly in advanced ages. The mean prevalence of this phenomenon in adults among western countries has been estimated 22% to 24% that about 47 million adult residents in the United States suffered MetS (1) (2). Beside, in some developed areas in Southeast Asia; this syndrome is prevalent in less than 14.2% of individuals (3). Among developing countries such as Iran and its neighbor countries, the prevalence of MetS has been significantly reported higher in a wide range between 10% (4) and 45% (5-7) Meanwhile, According to direct association between increase of age and prevalence of MetS, its higher occurrence in the elderly is more expectable as previously reported in Iranian older patients compared with younger ones and adolescents (8). Not only different metabolic definitional components of MetS

such as hyperglycemia, dyslipidemia, obesity, and hypertension have been considered as strong morbidities leading poor clinical conditions and impaired quality of life, but also combination of these underlying components can be potentially accompanied with higher incidence of atherosclerotic cardiovascular disorders, vascular inflammatory defects, and coagulative events compared with those without MetS (9). Although insulin resistance has been introduced as the main unifying mechanism responsible for increased incidence of ischemic events in MetS patients (10-12) but this mechanism and its-related processes has not been completely cleared. Furthermore, the role of MetS for predicting adverse events following cardiovascular therapeutic interventions has been recently revealed so that the association of MetS with mortality and morbidity both early and late after coronary artery bypass grafting (CABG) has been newly reported (13), however this evidence has not been obtained in some other surveys (14, 15). The present study came to address the value of MetS in predicting postoperative outcome following CABG.

Methods

In a retrospective study, a consecutive series of patients including 2010 subjects who underwent isolated CABG at Sina Hospital in Isfahan, Iran from 2007 to 2012 were reviewed. In this regard, all patients undergoing CABG concomitantly with other procedures were excluded. All patients underwent a full median sternotomy, and the operation was performed on cardiopulmonary bypass. This study was reviewed and approved by the Institutional Review Board of the Isfahan University of Medical Sciences. Baseline information was collected by reviewing hospital recorded files including demographic characteristics, anthropometric parameters (weight, height, waist circumference), risk profile (current smoking, hypertension, diabetes mellitus, hyperlipidemia, and renal failure, previous myocardial infarction, congestive heart failure, or angina pectoris, previous coronary interventions), and functional status according to The Canadian Cardiovascular Society (CCS) grading of angina pectoris. Also, intraoperative parameters such as type of surgery (elective or emergency), number of arteries or veins used as grafts, bypass time, and cross-clamp time were recorded. Postoperative complications during hospitalization were also recorded prospectively by trained personnel. The composite outcome of major adverse cardiac and cerebrovascular events (postoperative morbidity) was generated from the following individual events: myocardial infarction, cardiac arrhythmias, stroke, renal failure, and other cardiac-related problems. Along with clinical factors and for determining cases with MetS, a fasting plasma lipid profile (including total cholesterol, low-density lipoprotein [LDL] cholesterol, HDL cholesterol, and triglyceride levels) and blood pressure were also assessed in the resting state. MetS was diagnosed using the modified Adult Treatment Panel III of the National Cholesterol Education Program (16-18) criteria existing 1 to 3 months of CABG surgery: three of five among body mass index (BMI) greater than 30 kg/m^2, elevated triglycerides (≥150 mg/dL or drug treatment), reduced high density lipoprotein (HDL) (≤40 mg/dL in men, ≤50 mg/dL in women or drug treatment), elevated arterial blood pressure (≥130 mm Hg systolic, ≥85 mm Hg diastolic or drug treatment), and elevated fasting glucose (≥100 mg/dL or drug treatment). The study endpoint was to assess the value of MetS to predict postoperative MACCE (the composite outcome of major adverse cardiac and cerebrovascular events as the occurrence of myocardial infarction, cardiac arrhythmias, stroke, renal failure, and other cardiac-related problems).

Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's *t*-test or Mann-Whitney U test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. Predictors exhibiting a statistically significant relation with MACCE in the two groups in univariate analyses (with a p-value < 0.1) were taken for a multivariable logistic regression analysis to investigate their independence as predictors. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Overall, 2010 patients who underwent isolated CABG were studied that among them 24.7% suffered from MetS. Comparing two patients groups with and without MetS regarding baseline characteristics (table 1) showed higher distribution of male gender in those with MetS and also higher age in the latter group. Traditional risk factors for coronary artery disease including obesity, hypertension, diabetes, and hyperlipidemia were more prevalent in patients suffered MetS, while no differences were observed between the two groups with respect to heart failure, previous myocardial infarction, mean preoperative creatinine level, functional class based on CCS scoring, and previous history of revascularization. No significant differences were revealed between the groups in terms of intraoperative characteristics such as emergency surgery, intraoperative balloon pump use, the use of arterial conduits for grafts, as well as mean cross-clamp time and bypass surgery time (table 2). With regard to postoperative cardiac events (table 3), the most prevalent types of arrhythmias in both groups were atrial fibrillation, premature ventricular contractions, and premature atrial contractions respectively. No difference was found in the prevalence of postoperative arrhythmias between the two groups with and without MetS. Also, we found no significant differences in the prevalence of postoperative brain stroke, multi-organ failure, and dialysis due to postoperative renal failure. In total, early morbidity rate was 27.4% in MetS group and 27.8% in non-MetS group with no significant discrepancy (p=0.867). Using multivariable logistic regression modeling (table 3), we showed that MetS status could not predict postoperative morbidity. In this regard, advanced age, history of congestive heart failure, higher CCS scale, and longer cross-clamp time were main indicators of postoperative morbidity.

Table 1. Baseline characteristics and preoperative data

Characteristics	Group with MetS (n = 496)	Group without MetS (n = 1514)	P-value
Male gender	252 (50.8)	1122 (74.1)	< 0.001
Age, yr	66.73 ± 5.04	67.77 ± 5.69	< 0.001
Body mass index, kg/m^2	29.04 ± 4.30	26.00 ± 3.55	< 0.001
Obesity	217 (43.8)	172 (11.4)	< 0.001
Hypertension	470 (94.8)	603 (39.8)	< 0.001
Hyperlipidemia	474 (95.6)	675 (44.6)	< 0.001
Diabetes mellitus	410 (82.7)	305 (20.1)	< 0.001
Cigarette smoking	91 (18.3)	416 (27.5)	< 0.001
Congestive heart failure	10 (2.0)	31 (2.0)	0.996
Myocardial infarction	173 (34.9)	535 (35.3)	0.851
Serum creatinine	1.04 ± 0.35	1.02 ± 0.26	0.148
CCS score			0.213
0	28 (5.6)	134 (8.9)	
1	55 (11.1)	160 (10.6)	
2	310 (62.5)	892 (58.9)	
3	67 (13.5)	216 (14.3)	
4	36 (7.3)	112 (7.4)	
Previous CABG	1 (0.2)	4 (0.3)	0.999
Previous valve surgery	2 (0.4)	2 (0.1)	0.256
Previous PCI	24 (4.8)	64 (4.2)	0.563
Fasting blood sugar, mg/dl	132.56 ± 5.59	87.22 ± 4.90	< 0.001
Serum total cholesterol, mg/dl	182.45 ± 11.12	126.32 ± 9.98	< 0.001
Serum HDL, mg/dl	29.21 ± 4.45	42.74 ± 4.25	< 0.001
Serum creatinine level, mg/dl	1.01 ± 0.07	1.00 ± 0.12	0.887

CCS score

Table 2. Intraoperative and postoperative information

Characteristics	Group with METS (n = 496)	Group without METS (n = 1514)	P-value
Intraoperative data			
Emergency surgery	86 (17.3)	286 (18.9)	0.440
IABP use	17 (3.4)	34 (2.2)	0.146
Arteries used as graft	492 (99.2)	1490 (98.4)	0.199
Cross-clamp time	49.77 ± 21.45	51.32 ± 34.79	0.351
Bypass time	81.21 ± 30.06	81.05 ± 13.39	0.921
Postoperative complications			
Arrhythmias			
Atrial fibrillation	77 (15.5)	231 (15.3)	0.886
Premature atrial contractions	11 (2.2)	38 (2.5)	0.714
Premature ventricular contractions	23 (4.6)	84 (5.5)	0.433
Ventricular tachycardia	9 (1.8)	16 (1.1)	0.186
Others	25 (5.0)	82 (5.4)	0.746
Multi-system failure	5 (1.0)	13 (0.9)	0.784
Brain stroke	9 (1.8)	26 (1.7)	0.886
Dialysis	5 (1.0)	5 (0.3)	0.074
Early morbidity	136 (27.4)	421 (27.8)	0.867

Table 3. Main determinants of early morbidity in a multivariate regression model

Item	p-value	Odds Ratio	95% CI
Metabolic syndrome	0.977	1.006	0.682 – 1.484
Male gender	0.072	0.804	0.635 – 1.019
Age, yr	<0.001	1.062	1.042 – 1.081
Obesity	0.518	1.100	0.825 – 1.466
Hypertension	0.710	1.046	0.825 – 1.326
Hyperlipidemia	0.593	0.938	0.742 – 1.186
Diabetes mellitus	0.663	0.941	0.716 – 1.237
Cigarette smoking	0.739	0.958	0.743 – 1.235
Congestive heart failure	0.001	3.161	1.627 – 6.143
Myocardial infarction	0.373	1.103	0.889 – 1.319
CCS score	0.004	1.176	1.054 – 1.314
Previous PCI	0.442	0.807	0.467 – 1.394
Previous CABG	0.197	3.520	0.520 – 23.828
Emergency surgery	0.259	1.167	0.893 – 1.524
Cross-clamp time	0.020	0.990	0.982 – 0.998
Arteries used as graft	0.326	1.620	0.618 – 4.245
Bypass time	0.052	0.994	0.988 – 0.995

Hosmer – Lemeshow goodness of fit: $\chi^2 = 10.376$, p = 0.240

Discussion

At first, in our observation, the prevalence of 24.7% of patients who underwent CABG suffered from MetS that defined based on ATP III criteria modified for Asian population. This obtained ranged is nearly consistent with the prevalence of MetS in our general population without any evidences of cardiovascular disorders. The estimation of other studies regarding prevalence of MetS in CABG patients was however different compared with our observation so that in some of them, the prevalence was reported even higher than 42% (13, 14, 19, 20). In an overview of the MetS in young South African Asian patients with

myocardial infarction, the prevalence of the MetS depending on the definition, was as high as 69% (21). The obtained differences in the prevalence of this phenomenon might be originated from applying different definitional criteria of MetS and its components as well as might be due to variations in patients' selection criteria especially considering or ignoring some criteria interacted with coronary risk factors and MetS components.

We could not reveal any difference in early postoperative morbidity between the groups with and without MetS. This result may be explained by this fact that the patients without MetS might, of which each one is a risk factor for coronary artery disease. On the other hand, both groups with and without this syndrome have some components of METS that can be also considered as traditional risk factors for cardiovascular diseases. The results of previous studies were contradictory. A Japanese study showed that on multivariate analysis, the MetS had odds ratios of 2.47 for postoperative stroke and 3.81 for postoperative renal failure (20). Brackbill and colleagues showed that female patients with MetS undergoing CABG surgery were at increased risk for longer postoperative stays as well as for in-hospital death (13). It was also found by Angeloni et al. a strong association between METS and mortality both early and late after CABG surgery (18). Contrarily and in consistent with our study, Swart and colleagues showed no detrimental clinical effects of MetS on either the pre-operative risk factors or the outcome after CABG (14). Furthermore, Ozyazicioglu et al. did not demonstrate effective role of MetS for predicting postoperative death (15). These discrepancies can be also in order to difference in definition of postoperative morbidity and considering different postoperative serious events for its defining, or difference in time of following-up the patients. This discrepancy could be also related to employing different definitive criteria for METs so that not only the cutoff points for METs criteria are not similar in various populations, but also different definitions have considered waist circumference instead of BMI. These differences can potentially confound the association between preoperative METs and postoperative complications.

Although the association between MetS and early morbidity could not observe in our study, however some other studies showed its significant association with prolonged length of stay, in-hospital death, needing higher volume of blood transfusion, or with postoperative local or systemic infections (14, 22).

As a main study limitation, Because of notable missing on the data of waist circumference in our database, we had to use a definition of METs including BMI cutoff instead of waist circumference. Thus, we used the ATP III criteria for defining METs. Because of the existence different criteria for METs and thus different powers for predicting surgical outcome by considering these different criteria for METs, the use of two or more METS criteria in this study could result in high accuracy for predicting CABG.

In summary, our study confirmed the high prevalence of the MetS among patients who undergo CABG, it failed to demonstrate an effect of this syndrome on early postoperative morbidity. In fact, patients with the MetS were similarly at risk for postoperative complications in comparison with non- MetS group. However, the former group may be more exposed to longer hospital stay or in-hospital death that should be more evaluated in further studies. By confirming the role of METs for predicting CABG outcome, high-risk CABG groups for this poor outcome could be determined. However, because of the lack of association between CABG outcome and preoperative METS in our survey, considering other baseline variables (advanced age, heart failure, and function score) as well as prolonged cross-clamp time should be more considered for this predicting instead of METs or its components.

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Received: 13 November 2014
Accepetd: 6 March 2015
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