Metabolic Syndrome in Younger Patients with Acute Coronary Syndrome

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ABSTRACT

Metabolic Syndrome (MeS) has reached epidemic proportions among younger individuals. We sought to determine the prevalence of MeS and its influence on the risk of Acute Coronary Syndrome (ACS) in a younger patient population (≤50 years old). Consecutive patients aged < 50 years hospitalized with the first episode of ACS were categorized whether or not they meet the modified NCEP-ATP III criteria for MeS.1 Diabetic patients were excluded. The control group was comprised of subjects with a de novo diagnosis of CAD but without MeS or DM. The prevalence of MeS in the initial sample of 212 patients with ACS was 26% (N=55). Of the 75 subjects included in the final analysis, 55 patients had MeS (C1) and 20 did not (C2). Mean age, sex, LDL, and Framingham risk scores were not significantly different. Patients with MeS were significantly more likely to present with STEMI (OR 12.67, 95% CI 1.98-78.40, P=0.004), and have lower ejection fractions (45±12% vs. 58±3%, p=0.0001). Among patients younger than 50 years presenting with the first episode of ACS, the prevalence of MeS was high even in the absence of traditional cardiovascular risk factors. Increased incidence of STEMI and reduced EFs were more commonly seen among individuals with MeS.

Key words: Metabolic syndrome, acute coronary syndrome, coronary artery disease

Akut Koroner Sendromlu Genç Hastalarda Metabolik Sendrom

ÖZET

Metabolik sendrom (MeS) genç erişkinler arasında epidemik düzeylere ulaşmıştır. Çalışmamızda genç hasta (50 yaş altı) popülasyonunda MeS prevalasını saptamayı ve MeS'un akut koroner sendrom üzerindeki etkisini araştırmayı hedefledik. Akut koroner sendrom (AKS) nedeniyle ilk kez hastaneye yatırılan hastalara NCEP-ATP III kriterlerinin olup olmaması göz önüne alınarak MeS tanısı konuldu. Diyabetik hastalar çalışmadan dışlandı. Kontrol grubundaki hastalar diyabet veya metabolik sendrom tanısı olmayan bununla birlikte koroner arter hastalığı bulanan hastalardan oluşmaktaydı. Başlangıçta AKS bulunan 212 hastada MeS prevalansı %26 (n=55). Son analize dahil edilen 75 hastanın 55'inde MeS (C1) varken, 20 hastada MeS (C2) yoktu. Ortalama yaş, cinsiyet, LDL ve Framingham risk skorları açısından fark bulunamadı. MeS bulunan hastalar anlamlı olarak daha yüksek oranda STEMI ile başvurmuştur (OR 12.67, 95% CI 1.98-78.40, p=0.004) ve hastaların ejeksiyon fraksiyonları belirgin olarak daha düşüktü (45±12% vs. 58±3%, p=0.0001). Geleneksel kardiyovasküler risk faktörlerine sahip olmayan 50 yaş altı ilk AKS atağı ile başvuran genç hastalarda MeS prevalansı yüksek bulundu. MeS'u bulunan hasta grubunda STEMI insidansı ve EF düşüklüğü yüksekti.

Key words: Metabolik sendrom, akut koroner sendrom, kroner arter hastalığı

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INTRODUCTION

The current model of cardiovascular disease focuses on interventions aimed at achieving angiographic results while emphasizing arterial inflammation and endothelial dysfunction – which play central roles in determining the prognosis and progression of CVD – to a lesser degree. The INTERHEART study suggested that the risk of MI is almost entirely attributable to modifiable CV risk factors (1,2) including: dyslipidemia, smoking, HTN, psychosocial stress, DM, increased waist-hip ratio, physical inactivity, poor diet, and abstinence from alcohol. Many of these factors are clustered or find their beginnings in the Metabolic Syndrome (MeS). While much has been done to control cholesterol, HTN, and smoking as isolated entities, an effective means of directly combating MeS remains elusive.

MeS, a cluster of physiologic abnormalities that include obesity, insulin resistance, dyslipidemia, and pre-HTN, has reached epidemic proportions in the U.S. and worldwide, particularly among younger individuals. In the process, it has been added to the list of "traditional" markers of CV risk, since its individual components act synergistically to cause or accelerate the progression of atherosclerosis, (3) MeS is associated with a 2- to 4-fold increase in CV events, even when diabetic patients are excluded (4,5). MeS has been designated as a secondary target for behavioral intervention and/or aggressive risk factor management by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) (1). Although there is evidence to support increased CV morbidity and mortality in MeS, there is little data addressing the importance of isolated MeS as a risk factor in patients presenting with acute coronary syndrome (ACS). Further, CAD in younger age groups is a topic of increasing clinical interest owing to the potential for premature death and long-term disability (1). In this study, we report the prevalence of MeS in subjects aged ≤50 years with ACS and who underwent coronary angiography.

MATERIALS AND METHODS

The hospital charts of 212 consecutive patients, aged ≤50 years, hospitalized at Advocate Illinois Masonic Medical Center from January 2003 to December 2005 for ACS and found to have a >70% stenosis in at least one major epicardial vessel on coronary angiography, were reviewed. ACS was diagnosed if the patient had symptoms compatible with MI and had troponin I >0.05 ng/mL within 48 hours of admission. If the initial ECG showed ST-segment elevation in 2 contiguous leads or new LBBB, in conjunction with elevated troponin I, the syndrome was characterized as ACS with ST-elevation MI (STEMI). Patients with elevated troponin values (with or without ECG abnormalities apart from ST-segment elevation) were considered to have ACS with NSTEMI. Patients were then divided into 2 groups – cohort 1 (C1) if they have MeS or cohort 2 (C2) if they did not. The diagnosis of MeS was based on the modified NCEP-ATPIII MeS criteria (1). Peripheral venous blood samples were obtained from all participants after an overnight fast for glucose and lipid analysis. BMI was calculated using height and weight data obtained at the time of admission. Patients were diagnosed with HTN based on the JNC VII criteria (6). Those with a known history of CAD, impaired renal function (serum creatinine >1.4 or GFR <60 mL/min, DM (FBS >125 mg/dL) either previously diagnosed or diagnosed at presentation, or had insufficient data were excluded from the study.

Pertinent medical, family (premature CAD at <55 and <65 years of age in male and female first-degree relatives, respectively), and social (smoking, alcohol consumption, illegal substance use) histories were obtained for each pt. All available demographic, clinical, laboratory and angiographic data were also reviewed. Framingham risk scores (FRS) were calculated as well. Continuous variables were reported as mean ± SD and compared with independent-samples t-test. Categorical variables were reported as a frequency distribution and compared with Fisher's exact test. All statistical analyses were performed with SPSS version 17.0 (SPSS Inc, Chicago, IL).

RESULTS

From the initially sampled 212 patients, a total of 137 patients were excluded based on the exclusion criteria mentioned above. Of the remaining 75 patients, 55 had MeS and were included in the study cohort (C1). The control population (C2) was comprised of patients with a de novo diagnosis of CAD and absence of MeS or DM. The demographic and clinical characteristics of the subjects in both groups are illustrated in Table 1.

Of the patients in C1, 20 (36.4%) met 3 MeS criterion, 24 (43.6%) met 4, and 11 (20%) met all 5. The distribution

Table 1. *Patient Characteristics*

	Variable	MeS	p value
	Present (C1)	Absent (C2)	
Age	44 ± 5	41 ± 9	0.078
Male	38 (73)	14 (70)	ns
Smokers	37 (67)	7 (35)	0.017
HTN	30 (55)	6 (30)	0.072
Dyslipidemia	43 (78)	6 (30)	<0.0001
Family History			
HTN	22 (40)	10 (50)	0.598
DM	2 (4)	2 (10)	0.288
Hyperlipidemia	21 (38)	11 (55)	0.291
CAD	20 (36)	2 (10)	0.043
Medications at presentation			
Aspirin	15 (27)	6 (30)	0.816
B-blocker	11 (20)	6 (30)	0.367
ACEI/ARB	6 (11)	3 (15)	0.693
Statin	12 (22)	5 (25)	0.763
MeS Criteria			
Body Mass Index (kg/m2)	32 ± 6	27 ± 5	0.002
Blood pressure (mmHg)	144 ± 24	115 ± 15	0.001
Fasting blood sugar (mg/dL)	137 ± 61	98 ± 18	0.141
HDL (mg/dL)	32 ± 12	39 ± 14	0.036
Triglycerides (mg/dL)	201 ± 135	123 ± 52	0.015
Presented with STEMI	22 (40)	1 (5)	0.004
Ejection Fraction (%)	45 ± 12	58 ± 3	0.0001
Framingham Risk Score	10 ± 5	11 ± 5	0.386

Legend: ACE-angiotension converting enzyme inhibitor, ARB-angiotension receptor blocker, C1- cohort 1 or patients with metabolic syndrome, C2-cohort 2 or patients without metabolic syndrome, CAD- coronary artery disease, DM- diabetes mellitus, HTN- hypertension, MeS- metabolic syndrome, STEMI- ST-elevation myocardial infarction.

of MeS criteria in C1 were as follows: 45 patients (81.8%) had low HDL, 42 (76.4%) had FBS ≥100 mg/dL, 46 (83.6%) had BMIs >25 kg/m², 35 (63.6%) had TG chol ≥150 mg/dl, and 43 (78.2%) had BP ≥130/85 mm Hg. The distribution of MeS criteria in C2 were as follows: 4 patients (20%) had low HDL levels, 3 (15%) had FBS ≥100 mg/dL, 6 (30%) had BMIs >25 kg/m², 3 (15%) had TG chol ≥150 mg/dl, and 0 (0%) had BP ≥130/85 mm Hg. The lipid analysis for both cohorts is shown in Table 2. There were no significant differences between the two groups, excluding TG chol and HDL. Compared to the control group, C1 patients were more likely to be smokers, present with STEMI (OR 12.67, 95% CI 1.98-78.40, p=0.004) and have lower EF (45±12% vs 58±3%, p=0.0001).

DISCUSSION

In our study, 26% of patients had MeS. This prevalence was in line with the overall 23% prevalence found in the Third National Health and Nutrition Examination Survey, which included patients from 20 years and older (7).

Our study population included younger patients (aged <50 years) presenting with their first episode of ACS. In a similar study, Chung et al. reported that MeS is highly prevalent in patients aged < 45 years presenting with ACS; however, the incidence of STEMI was not significantly different in patients with and those without MeS (p=0.825) (8).

An interesting finding in the younger pt population in our study was the fact that those with MeS more often presented with STEMI and had lower EFs. This raises questions as to the nature of coronary lesions in MeS patients versus the rest of the coronary population. Are MeS patients more prone to total occlusions owing to softer, more labile plaques? Do they end up with worse LV function post-MI due to subclinical chronic underlying systolic/diastolic dysfunction? The increasing occurrence of CAD in the young has serious implications on morbidity, premature death, and long-term disability (5,9,10). Current guidelines may be inadequate to identify younger adults at higher risk for vascular disease because they are based on near-term global risk

Table 2. Lipid Analysis

Variable	MeS		p value
	Present (C1)	Absent (C2)	
Total Cholesterol	195 ± 58	182 ± 50	0.495
LDL (mg/dL)	128 ± 50	113 ± 46	0.358
HDL (mg/dL)	32 ± 12	39 ± 14	0.036
Triglycerides (mg/dL)	201 ± 135	123 ± 52	0.015
Non-HDL (mg/dL)	160 ± 57	143 ± 52	0.343
Total Chol/HDL (mg/dL)	6.6 ± 2.6	5.1 ± 2.1	0.086
Triglycerides/HDL (mg/dL)	7.1 ± 5.3	4.1 ± 1.9	0.070

assessment criteria (i.e., the FRS), which are heavily dependent on age. Most younger patient populations studied notably lacked traditional CV risk factors, it was the case in this report (5). The FRS was almost equal for both cohorts despite significantly more STEMIs occurring in C1. The addition of MeS to traditional criterion may enhance the detection of high risk individuals, beyond those identified by conventional CV risk scores. Several reasons have been postulated to explain the heightened CV risk associated with MeS, including higher levels of fibrinogen, (11) plasminogen activator inhibitor-1, and excessive smaller LDL cholesterol particles.

Our study population had a 52% incidence of smoking, below the 61 to 93% incidence in multiple previous studies, making it a less important contributor to their presentation (9,12,13). Again suggesting MeS may play a significantly more important role in the progression of CV disease in this age group.

The importance of MeS from a clinical and public health perspective is twofold: (1) as a contributor to disease progression, before the development of clinically detected CAD or DM; (2) its relevance in patients who have already experienced a coronary event, as a predictor of future risk. Studies have shown an association between more advanced vascular damage in patients with MeS and vascular disease than those without MeS, possibly worsening their prognosis (11,14,15). MeS also has been found to be a predictor of increased CV event recurrence (16). The economic burden of attempting secondary prevention in such a large population is staggering and potentially avoidable, if started early enough and attempted in a vigorous fashion.

Study limitations: Our series was comprised mostly of men and since we utilized a modified definition of MeS based on ATPIII and WHO guidelines this may have had

an impact on the selection of the sample. Furthermore, no angiographic analysis was performed for specific lesion features between both cohorts.

Newer data have called into question the usefulness of MeS in predicting CAD. The argument is that the inclusion of MeS adds nothing to current prediction models (i.e., FRS) (17) However, those models are notoriously unreliable in women and younger patients (5,17) and in fact, the FRS was not statistically significant in our series. It is imperative that a more practical and cohesive risk factor assessment for young patients is developed, which include MeS or its components.

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