

Metabolic Syndrome and Angiographic Coronary Artery Disease Prevalence in Association with the Framingham Risk Score

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Abstract

Background: The association of metabolic syndrome with coronary artery disease (CAD) has been studied extensively. However, little is known about the effect of Framingham risk score (FRS) and metabolic syndrome components on the association of metabolic syndrome with angiographically significant CAD. Our aim was to investigate whether that relationship is influenced by individual's 10-year CAD risk profile as assessed by FRS. Furthermore, we sought to elucidate whether metabolic syndrome is associated with angiographically significant CAD independently of its individual components.

Methods: We studied a consecutive sample of 150 patients undergoing coronary angiography for the evaluation of chest pain. Metabolic syndrome was defined according to the revised National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, and the 10-year CAD risk was estimated by the FRS.

Results: Metabolic syndrome patients had a 2-fold higher CAD prevalence compared to those without metabolic syndrome [odds ratio (OR), 2.004; 95% confidence interval (CI), 1.029–3.905] but this finding was attenuated after adjustment for FRS (OR, 1.770; 95% CI, 0.872–3.594). Stratification of patients into three groups according to FRS revealed that metabolic syndrome predictive ability was confined in those being at <10% 10-year CAD risk. Including metabolic syndrome and its individual components into the same logistic regression model, only the glucose criterion was an independent predictor of angiographically significant CAD (OR, 4.137; 95% CI, 1.477–11.583).

Conclusions: Metabolic syndrome is an independent determinant of angiographically significant CAD only among those individuals at low 10-year risk for future coronary events. Individual components of the syndrome, such as impaired fasting glucose, have a stronger association with CAD than the syndrome as a whole.

Introduction

THE TERM METABOLIC SYNDROME is used to describe the constellation of coronary artery disease (CAD) risk factors, such as abdominal obesity, nontraditional dyslipidemia [ie, low high-density lipoprotein cholesterol (HDL-C) and high triglycerides levels and the presence of small, dense low-density lipoprotein cholesterol (LDL-C) particles], impaired fasting glucose levels, and elevated blood pressure. These metabolic abnormalities tend to cluster in some individuals in a frequency greater than chance expectation, and it has been hypothesized that the underlying pathophysiological disorder is insulin resistance.¹ As sedentarism and the western-type diet are widespread across the

world, obesity, diabetes mellitus, and metabolic syndrome become epidemic. According to the Third National Health And Nutrition Examination Survey (NHANES III), the age-adjusted prevalence of metabolic syndrome is 23.7%, which means that, using 2000 census data, 47 million U.S. citizens have the syndrome.² Even more worrisome is that this condition is increasing at an alarming rate in young people with a prevalence of 28.7% among adolescents whose body mass index (BMI) is $\geq 95^{\text{th}}$ percentile, translating into 910,000 U.S. carriers of metabolic syndrome in that age group.³ Data from large prospective trials on apparently healthy subjects suggest that the presence of metabolic syndrome correlates with incident diabetes,⁴ increased cardiovascular disease risk,^{5–8}

and excess cardiovascular and total mortality.⁹ Accordingly, the Adult Treatment Panel III (ATP III) recognized the metabolic syndrome as a secondary target of risk-reduction therapy, after the primary target, LDL-C, has been reached.¹⁰

There is evidence, however, disputing the validity of the metabolic syndrome as a marker of future cardiovascular events. In a prospective angiographic study among postmenopausal women, only diabetes, but not the metabolic syndrome, was associated with significant reduction of the coronary lumen diameter and future cardiovascular adverse events.¹¹ Evidence from a cohort of American Indians without baseline diabetes or cardiovascular disease suggests that metabolic syndrome can predict only diabetes independently, but not future cardiovascular events,¹² whereas follow-up of diabetic individuals revealed that metabolic syndrome is not an independent prognostic marker of cardiovascular and total mortality.¹³ It was also suggested that metabolic syndrome is inferior to the Framingham risk score (FRS) in future cardiovascular adverse events prediction^{14,15} and that the syndrome itself conveys no additional risk than the sum of its parts.¹⁶ This apparent discrepancy concerning metabolic syndrome and its clinical implications is summarized by a joint statement of the American Diabetes Association and the European Association for the Study of Diabetes, suggesting that health-care providers should avoid labelling patients with the term metabolic syndrome, because this might create the impression that the metabolic syndrome denotes a greater risk than its components, or that it is more serious than other cardiovascular disease risk factors, or that the underlying pathophysiology is clear.¹⁷

In the present study, we aimed to evaluate the association of metabolic syndrome with angiographically significant CAD. We also investigated whether that relationship of metabolic syndrome with CAD is influenced by individual's 10-year CAD risk profile as assessed by FRS. Finally, we sought to elucidate whether metabolic syndrome is associated with angiographically significant CAD independently of its individual components.

Materials and Methods

Study population

Our study population included a sample of 150 consecutive individuals who presented to the emergency department of our center (AHEPA University hospital, Thessaloniki, Greece) from March, 2006, until May, 2006, complaining about chest pain. None of the patients was diagnosed with myocardial infarction at his/her presentation and no one had any history of myocardial infarction or coronary intervention in the past (ie, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting). All subjects had a positive stress test and/or intermediate- to high-risk angina, and they were referred for coronary angiography.

Before entering the catheterization laboratory, a detailed medical history was recorded concerning demographics, socioeconomic status, family history of cardiovascular disease, smoking habits and alcohol consumption, dietary pattern, past and current medical conditions, and specific treatment being followed. Next, each one was subjected to a thorough physical examination. BMI was calculated by dividing weight in kilograms by the square of height in meters (kg/m^2). Waist circumference was calculated as the

average of two measurements taken after inspiration and expiration at the highest point of iliac crest. Blood pressure was assessed with the patient being in a sitting position, and the average of three measurements was recorded. Subjects were considered as hypertensive if their blood pressure exceeded 140/90 mmHg or if they were under antihypertensive treatment. A diagnosis of diabetes was made if fasting blood glucose levels were >125 mg/dL or in the case of treated diabetes. A family history of CAD was considered to be present if a subject had any first-degree relatives with a history of CAD or sudden cardiac death prior to age of 55 years for males and to 65 years for females.

The study protocol was approved by the Institutional Medical Ethics Committee and all participants provided an informed consent.

Blood tests for lipids

All patients had fasted for at least 8 h, and venous blood was drawn through the antecubital vein without using a tourniquet, approximately 30 min before the catheterization procedure. The samples were centrifuged at $3,000 \times g$ for 10 min at ambient temperature. Serum triglycerides, total cholesterol, HDL-C, and glucose were determined with standard enzymatic procedures. Serum LDL-C was calculated using Friedewald formula.

Metabolic syndrome definition

A number of different definitions for the diagnosis of metabolic syndrome have been proposed. Among them the most commonly used are those by the World Health Organization (WHO), by the International Diabetes Federation (IDF), and by the National Cholesterol Education Program (NCEP) ATP III. In our study, we applied the revised NCEP ATP III criteria.¹⁸ NCEP-defined metabolic syndrome was associated more strongly with future cardiovascular events compared with IDF criteria.¹⁹ Individuals identified with metabolic syndrome according to IDF criteria, but not by NCEP definition, were no more insulin resistant²⁰ and showed no increased cardiovascular disease prevalence²¹ than the metabolic syndrome-free subjects. In contrast to IDF criteria, individuals with NCEP-defined metabolic syndrome had a persistently higher prevalence of cardiovascular disease compared with the general population, irrespective of their diabetic status.²¹ Concerning the WHO and the NCEP definitions, despite the fact that there was a considerably high concordance between the two definitions, the simpler NCEP definition was associated with a greater risk for all-cause and cardiovascular mortality, especially in lower-risk subjects.²²

According to the revised NCEP ATP III criteria, one had the syndrome if at least three of the following occurred: Blood pressure $\geq 130/85$ or under antihypertensive treatment, triglyceride levels ≥ 150 mg/dL, HDL-C levels <40 mg/dL if men and <50 mg/dL if women, waist circumference >102 cm if men and >88 cm if women, and fasting glucose levels ≥ 100 mg/dL or treated diabetes.

FRS assessment

The FRS is a validated risk scoring system for 10-year CAD risk prediction.²³ The risk factors that are employed in that score include age, total cholesterol, HDL-C, systolic

blood pressure (SBP), and smoking with gender specific cut-off points. SBP values are graded differentially depending on individual's use of antihypertensive drugs or not. Total cholesterol and smoking habit are assigned coefficients in relation to the patient's age group. One is characterized at low (<10%), moderate (10%–20%), or high (>20%) 10-year CAD risk according to the total score achieved.

Coronary angiography

Coronary angiograms were evaluated by two authors, who were blinded to the study plan and to each other. A luminal narrowing of $\geq 50\%$ in at least one major epicardial coronary artery was considered as significant CAD. Patients were further classified as having no, one, two, or three vessels disease. The last two categories were considered as one because of the small number of patients. Left main coronary artery involvement was considered as two-vessel disease.

A more thorough description of CAD severity was made by using three different angiographic scoring systems, such as the Gensini score,²⁴ extent score,²⁵ and arbitrary index.²⁶ For the calculation of the Gensini score, the coronary artery tree was divided into 15 segments according to Austen's nomenclature²⁷: Left main coronary artery, right coronary artery was divided into four segments (proximal, middle, distal, and posterior descending artery), left anterior descending into five segments (proximal, middle, distal, first, and second diagonal branch), and left circumflex into five segments (proximal, distal, first, second, and third obtuse marginal branch). An anatomical coefficient was assigned to each coronary artery segment depending on the functional significance of the area supplied by that segment. This coefficient was: 5 for the left main coronary artery; 2.5 for the proximal segments of left anterior descending and circumflex; 1.5 for the middle segment of left anterior descending; 1 for the distal segments of left anterior descending and circumflex, as well as for all the right coronary artery segments, posterior descending artery, first diagonal, and first obtuse marginal branch; and 0.5 for the second diagonal and the second obtuse marginal branch. Each stenosis was classified as grade of 1 for 1%–49% reduction in lumen diameter, 2 for 50%–74%, 3 for 75%–99%, and 4 for total occlusion (100%). The stenosis grade was multiplied with the respective anatomical coefficient in each segment, and all segmental products were added together to give a total score out of the theoretical maximum of 82.

The extent score was defined as the percentage of analyzed segments with luminal narrowing of 25% or more. The extent score indicated the angiographically apparent extent of the coronary artery wall abnormalities throughout the coronary bed ranging from 0 to 1.

The arbitrary index was calculated by adding all stenoses (in percentage), expressed in SI units (eg, 50% = 0.50).

Statistical analyses

Continuous variables were expressed as mean \pm standard deviation (SD) and categorical variables as absolute numbers and percentages. The unpaired Student *t*-test and Mann–Whitney U-test were used for comparison of means between two groups for normally and nonnormally distributed variables, respectively. Accordingly, the one-way analysis of variance (ANOVA) and Kruskal–Wallis H test

were used for comparison of means among three or more groups. Comparison between proportions was performed using chi-squared analysis. Logistic regression analysis was carried out to evaluate the impact of the metabolic syndrome on angiographically significant CAD prevalence, controlling for FRS or metabolic syndrome components. For all tests, a two-sided $P < 0.05$ was considered to be statistically significant. SPSS statistical analysis software version 15.0 (SPSS Inc. Chicago, IL) was used to conduct all statistical analyses.

Results

Out of 150 patients, the metabolic syndrome was present in 92 (61.3%), whereas the remainder 58 (38.7%) did not meet the criteria of metabolic syndrome. Table 1 outlines the demographic, clinical, and biochemical characteristics of the patients according to metabolic status. Not surprisingly, individuals with metabolic syndrome, compared to those without the syndrome, had significantly larger waist circumference measurements together with higher values of BMI, higher levels of triglycerides, fasting glucose, and glycosylated hemoglobin (HbA1c), and lower concentrations of HDL-C. Blood pressure levels did not differ significantly between groups, although a trend toward higher values among metabolic syndrome patients was observed, possibly due to the high prevalence of arterial hypertension in the population under study. Furthermore, a significantly higher prevalence of female gender and diabetes mellitus was documented in the metabolic syndrome group, whereas a smoking habit was much more prominent among non-metabolic syndrome individuals.

The number of metabolic syndrome components per subject (ie, metabolic score), followed a nearly Gaussian distribution, slightly skewed to the right with the most frequent category formed by those with three components of the syndrome (Fig. 1A). The most frequent metabolic syndrome component was hypertension with a prevalence of 85.3%, whereas the less frequent one was the low HDL-C observed in 33.8% of the patients (Fig. 1B).

Association of metabolic syndrome with angiographically significant CAD

According to coronary angiographic findings, 83 (55.3%) individuals had angiographically significant CAD and 67 (44.7%) had angiographically minor or no stenoses. Figure 2 shows CAD prevalence as well as the number of diseased vessels in relation to metabolic syndrome status. Metabolic syndrome patients have a 2-fold higher CAD prevalence [odds ratio (OR), 2.004; 95% confidence interval (CI), 1.029–3.905] compared to their non-metabolic syndrome counterparts. Although metabolic syndrome patients outnumbered non-metabolic syndrome individuals concerning one vessel (31.9% vs. 20.7%) and two or three vessels disease (29.7% vs. 24.1%), this finding was not statistically significant ($P = 0.122$). For a more detailed description of the atherosclerotic burden, three different angiographic indexes were used, namely Gensini score, extent score, and arbitrary index. There was a trend toward higher scores for each of the above three angiographic indexes among metabolic syndrome patients (Table 2).

TABLE 1. DEMOGRAPHICS, CLINICAL, AND BIOCHEMICAL CHARACTERISTICS OF THE PATIENTS IN RELATION TO METABOLIC STATUS

	Metabolic syndrome (+) <i>n</i> = 92	Metabolic syndrome (-) <i>n</i> = 58	<i>P</i>
Age (years)	63.90 ± 8.99	61.64 ± 11.93	0.454
Gender (men)	52 (56.5)	45 (77.6)	0.009
Family history of CAD	24 (26.4)	15 (26.8)	0.956
Smoking	45 (48.9)	39 (67.2)	0.028
Pack × years ^a	55.05 ± 35.86	44.13 ± 31.37	0.361
Body mass index (kg/m ²)	29.56 ± 3.20	27.28 ± 3.31	< 0.001
Waist circumference (cm)	103.98 ± 8.32	96.52 ± 9.61	< 0.001
Systolic blood pressure (mmHg)	143.10 ± 23.45	136.14 ± 26.32	0.099
Diastolic blood pressure (mmHg)	80.49 ± 12.45	77.81 ± 13.76	0.373
Diabetes	50 (54.3)	10 (17.5)	< 0.001
Fasting glucose (mg/dL)	132.44 ± 46.67	104.07 ± 29.35	< 0.001
HbA1c (mg/dL)	5.89 ± 1.54	4.90 ± 1.01	< 0.001
Total cholesterol (mg/dL)	182.66 ± 45.23	184.69 ± 39.85	0.780
Triglycerides (mg/dL)	147.99 ± 57.93	101.95 ± 36.48	< 0.001
LDL-C (mg/dL)	106.20 ± 37.49	109.37 ± 37.00	0.615
HDL-C (mg/dL)	47.12 ± 12.63	54.93 ± 15.99	0.001
Non-HDL-C (mg/dL)	135.87 ± 42.38	129.76 ± 38.26	0.375

^aVariable calculated only for current smokers.

Data are mean ± SD or absolute numbers (%) within each metabolic syndrome group.

Statistically significant *P* values are in boldface.

Abbreviations: CAD, coronary artery disease; HbA1c, glycosylated hemoglobin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SD, standard deviation.

Association of metabolic syndrome with CAD across FRS categories

To test whether metabolic syndrome presence correlates with CAD independently of conventional risk factors considered by FRS, a multivariate analysis was performed. After adjustment for FRS, metabolic syndrome was no more a determinant of CAD prevalence (OR, 1.770; 95% CI, 0.872–3.594). We further stratified our study population into three groups

on the basis of 10-year CAD risk as derived by the FRS: Low risk (<10%), moderate risk (10%–20%), and high risk (>20%). The number of the patients in each group was 49 (32.5%), 73 (49%), and 28 (18.5%), respectively. Metabolic syndrome was significantly associated with CAD in individuals with low 10-year CAD risk (OR, 4.577; 95% CI, 1.216–17.223). However, as 10-year CAD risk profile worsened, the association of MS with CAD was attenuated and no longer significant (Fig. 3A). Likewise, metabolic syndrome was associated with a greater

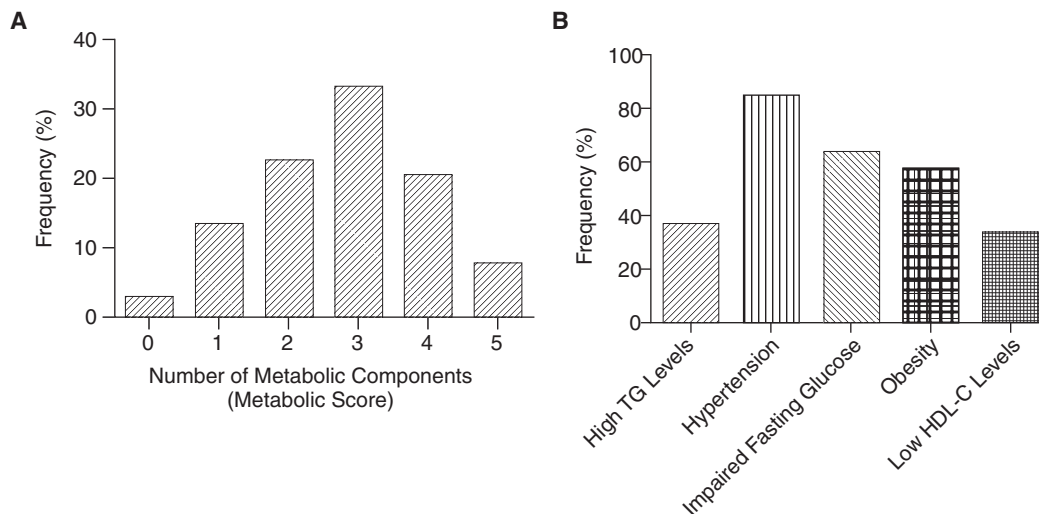


FIG. 1. (A) Distribution of the number of the metabolic syndrome components per subject, that is, metabolic score among study participants. Data are presented as percentages. (B) Prevalence of each metabolic syndrome component among the patients. Data are presented as percentages. TG, Triglycerides; HDL-C, high-density lipoprotein cholesterol.

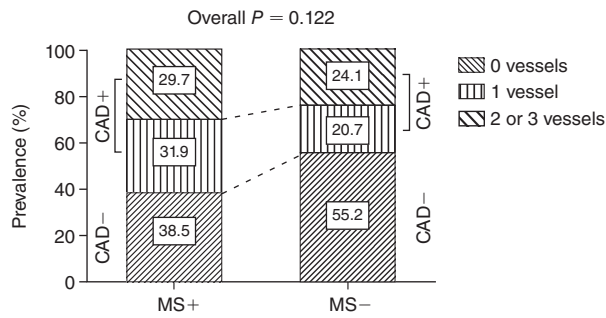


FIG. 2. CAD and number of diseased vessels prevalence in metabolic syndrome and non-metabolic syndrome patients. Data are percentages within each metabolic syndrome group. The *P* value represents the overall trend resulting from comparison among all groups. Abbreviations: CAD, coronary artery disease; MS, metabolic syndrome.

TABLE 2. ANGIOGRAPHIC SCORES IN METABOLIC SYNDROME AND NON-METABOLIC SYNDROME INDIVIDUALS

	Metabolic syndrome (+)	Metabolic syndrome (-)	<i>P</i>
Gensini score	7.14 ± 7.05	6.49 ± 8.39	0.18
Extent score	0.16 ± 0.15	0.15 ± 0.17	0.22
Arbitrary index	1.70 ± 1.67	1.42 ± 1.75	0.16

Data are mean ± SD. Abbreviation: SD, standard deviation.

prevalence of angiographically diseased vessels only in low 10-year CAD risk subjects (Fig. 3B).

Association of metabolic syndrome with CAD adjusting for its own components

Another issue that deserves further elucidation is whether metabolic syndrome correlates with CAD prevalence independently of its own constituents. Metabolic syndrome components were tested for multicollinearity before entered in the same regression model. The only significant intercorrelations observed were those between hypertriglyceridemia with low HDL levels ($r = 0.280, P = 0.001$), hypertriglyceridemia with impaired fasting glucose ($r = 0.203, P = 0.015$), and between high blood pressure with waist circumference criterion ($r = 0.200, P = 0.017$). However, the above correlation coefficients were weak ($r < 0.3$), thus not significantly blunting the relationship between each independent variable with CAD prevalence. Multivariate analysis revealed that when metabolic syndrome was included in the same regression model together with its components, it was not

an independent determinant of angiographically significant CAD prevalence. Concerning individual metabolic components, only impaired fasting glucose was independently associated with angiographically significant CAD (Table 3).

Discussion

Metabolic syndrome and CAD prevalence and severity

In our study, metabolic syndrome prevalence was 61.3%, which is almost three times higher than that estimated by large-scale epidemiologic surveys, such as NHANES III.²⁸ Our subjects, however, comprised a highly selected group of patients complaining of chest discomfort and were referred for coronary angiography, which justifies the clustering of various metabolic syndrome components. Our findings are much more consistent with those of angiographic studies yielding a metabolic syndrome prevalence of 49.2%,²⁹ or even 66%.³⁰

According to our results, the presence of metabolic syndrome was positively correlated with angiographically significant CAD prevalence. This is in concordance with other angiographic studies reporting a significantly higher prevalence of CAD among patients with metabolic syndrome compared to their non-metabolic syndrome counterparts.^{30,31} Our findings are also confirmed by epidemiologic surveys exploring the relationship between metabolic syndrome and

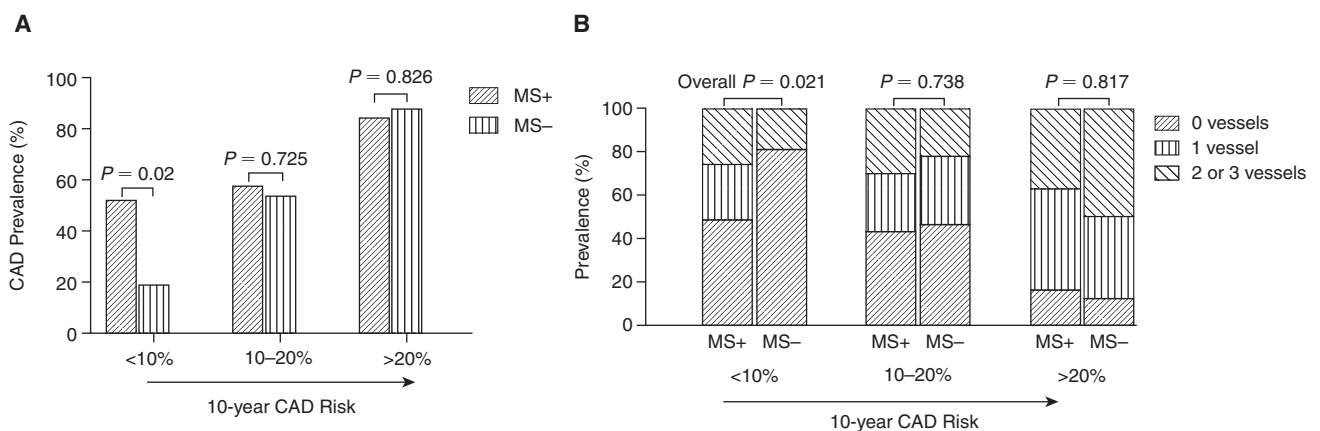


FIG. 3. (A) CAD prevalence (%) in metabolic syndrome and non-metabolic syndrome patients stratified by Framingham risk score (FRS) into three groups. (B) Prevalence of the number of diseased vessels in metabolic syndrome and non-metabolic syndrome patients across the three FRS groups. Data are percentages within each metabolic syndrome group. The *P* value represents overall trend resulting from comparison among all groups per FRS category. CAD, Coronary artery disease; MS, metabolic syndrome.

TABLE 3. ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR CAD DERIVED FROM A LOGISTIC REGRESSION MODEL INCLUDING METABOLIC SYNDROME TOGETHER WITH ITS INDIVIDUAL COMPONENTS

	OR	95% CI	P
Metabolic syndrome	0.697	0.164–2.964	0.625
Hypertension	1.305	0.447–3.808	0.626
High triglycerides	1.855	0.769–4.471	0.169
Obesity	0.534	0.203–1.404	0.203
Low HDL-C	1.368	0.575–3.255	0.478
Impaired fasting glucose	4.137	1.477–11.583	0.007

Statistically significant *P* values are in boldface.

Abbreviations: CAD, coronary artery disease; OR, odds ratio; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol.

prevalent CAD,²¹ as well as by studies using other methods for CAD documentation, such as measurement of the extent of coronary artery calcification.³²

In our study, patients with metabolic syndrome had a tendency for greater atherosclerotic burden both in terms of number of diseased vessels and angiographic scores, but this difference failed to reach statistical significance. Concerning the association of metabolic syndrome with CAD severity, the bibliographic data are conflicting. There are studies reporting a significantly higher cumulative coronary artery stenosis score,²⁶ as well as extension and severity scores,³³ in the presence of metabolic syndrome. On the other hand, there is evidence supporting similar prevalence of three-vessel disease among metabolic syndrome individuals and those without the syndrome²⁹ and no significant association between metabolic syndrome and scores combining the extent and severity of angiographic findings.³⁴

Our inability to demonstrate a clear association of metabolic syndrome with CAD severity may be attributed in part to the high prevalence of metabolic syndrome, which underscores its clinical importance. Also of note, individuals who did not meet metabolic syndrome diagnostic criteria, but with one or two metabolic syndrome components, were still at increased risk for CAD compared to non-metabolic syndrome subjects with no metabolic abnormalities at all. The small number of women participating in our study (35.3%) may also play a role, because some authors suggest that metabolic syndrome impacts CAD prevalence and total atheroma burden to a greater extent in females than in males.^{33,35,36} The limitations of metabolic syndrome diagnostic criteria could also have a significant effect on populations being identified. For instance, in a prospective case-control study, IDF-defined metabolic syndrome was significantly associated both with CAD prevalence and its angiographic extent, whereas no such relationship was found using the NCEP ATP III definition.³⁷

Metabolic syndrome and CAD in relation to 10-year CAD risk

We analyzed the effect of metabolic syndrome on CAD prevalence in the setting of established risk factors involved in FRS. Multivariate analysis revealed that metabolic syndrome was not an independent predictor of CAD prevalence after adjustment for FRS (OR, 1.770; 95% CI, 0.872–3.594).

By using FRS, our patients were stratified into those having <10%, 10%–20%, and >20% estimated 10-year CAD risk. Then, we assessed separately for each group the relationship between metabolic syndrome and CAD prevalence as well as the number of diseased vessels. We found for the first time that metabolic syndrome had a significant impact on CAD prevalence and on the number of diseased arteries only among those characterized as low-risk patients according to FRS. This novel finding indicates that metabolic syndrome could reliably be used to predict CAD in low-risk patients referred to coronary angiography.

Metabolic syndrome versus its own components

An increasing amount of studies suggest that metabolic syndrome conveys no additional predictive information beyond its components, casting doubt on its clinical utility or even on its existence as a discrete entity. In The Pittsburgh Epidemiology of Diabetes Complications Study, the individual components of metabolic syndrome, rather than their assemblage, were stronger predictors of the study end points. In fact, microalbuminuria, a component of the WHO definition of metabolic syndrome, provided better prediction than the whole syndrome.³⁸ Prospective data from the Caerphilly and Speedwell populations suggest that metabolic syndrome was not able to predict CAD, after adjustment for traditional and metabolic risk factors.³⁹ Data derived from NHANES III participants aged ≥ 50 years suggest that when NCEP-defined metabolic syndrome and its individual metabolic abnormalities are incorporated into the same multivariate model, only HDL-C, blood pressure, and diabetes are still significantly associated with CAD prevalence.⁴⁰ In the current study, including metabolic syndrome together with its own components into the same multivariate model, we revealed that only the glucose criterion, but not the syndrome *per se*, was independently associated with CAD. Notably, diabetes was much more prevalent among metabolic syndrome subjects compared to non-metabolic syndrome individuals (54.3% vs. 17.5% respectively, $P < 0.001$). It is very likely that the risk associated with metabolic syndrome is mediated mainly through impaired fasting glucose and probably by a significant overlap between diabetes and the metabolic syndrome.

Study limitations

Our study is limited by the small number of participants, which explains in part the weak associations observed among the tested variables and the wide confidence intervals as well. Our study participants were a consecutive sample of individuals visiting our center with chest pain and suspected myocardial ischemia that prompted coronary angiography. These subjects were self-selected rather than randomly selected by us, a fact introducing a selection bias. Moreover, because our study did not include a representative sample of Thessaloniki's inhabitants, our results cannot be extrapolated to the general population. As a result, due to the cross-sectional design of our work, we cannot infer causality from the associations detected. These results are, however, indicative and further prospective studies are warranted to demonstrate whether individuals without the metabolic syndrome are indeed at lower cardiovascular risk than those with the syndrome.

Coronary atherosclerotic lesions were evaluated by visual estimation of coronary angiograms by two authors blinded to each other and to the study protocol. However, individuals with chest discomfort and normal coronary lumens on angiography may still have some degree of atherosclerosis, which is only detectable by intravascular ultrasound. To overcome this limitation, we focused on angiographically significant lesions resulting in a luminal narrowing >50%. Flow-limiting lesions can be reliably assessed by angiography and are associated with a lower interobserver variability. Two out of five metabolic syndrome components, that is, low HDL-C levels and high blood pressure, are involved in FRS assessment too. Hence, the two definitions are partly intercorrelated. However, the main scope of our study was to stratify our subjects into low, medium, and high risk for CAD according to FRS rather directly comparing the ability of the two definitions to predict the angiographic outcome. A significant proportion of the patients were under lipid-lowering, antihypertensive, and antidiabetic treatment, which may interfere with the patients' biochemical characteristics and potentially with the assessment of their metabolic profile.

Conclusions

Metabolic syndrome correlates with CAD only in individuals with low 10-year CAD risk, whereas this association is blunted in moderate- or high-risk subjects. Moreover, the association of metabolic syndrome with CAD is attenuated after adjustment for its components, suggesting that metabolic syndrome as a whole does not add more prognostic value than each of its components. In fact, individual components of the syndrome, such as impaired fasting glucose, exhibit a more pronounced association with prevalent CAD than with the syndrome as a whole. Therefore, it is very likely that clinicians may gain more benefit from preventing or managing the individual abnormalities of the metabolic syndrome, especially elevated blood glucose levels, than diagnosing metabolic syndrome itself.

Author Disclosure Statement

No competing financial interests exist.

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