Metabolic syndrome and coronary artery disease in young Egyptians presenting with acute coronary syndrome

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Rationale
The aim of this study is to determine the relationship between metabolic syndrome and the extent of coronary artery disease (CAD) in young adults presenting with acute coronary syndrome.

Background
Metabolic syndrome is associated with subsequent development of type II diabetes mellitus and cardiovascular disease. Individuals with metabolic syndrome are at a higher risk of developing myocardial infarction and CAD.

Patients and methods
This study was carried out at Kasr Al Ainy Hospital at Cairo University and the Sohag Specialized Cardiac and Digestive System Center. One hundred and twenty-two patients presented with acute coronary syndrome during the period of the study from January 2011 to January 2012. Eighty-five were men (69.7%) and 37 were women (30.3%). Patients were classified into two groups according to the presence or absence of metabolic syndrome to determine the effect of metabolic syndrome on severity of coronary lesions in comparison with nonmetabolic patients. Correlation was assessed between the number of metabolic risk components and coronary lesion severity using the SYNTAX score.

Results
The metabolic risk score was determined; patients with a significant metabolic score of at least 3 risk score constituted 66.4% of the total cohort (n = 81 patients).
Patients were subjected to coronary angiography. Totally occluded vessels were found in 33.3% of metabolic syndrome patients and in 26.8% of non metabolic syndrome patients ($P < 0.05$). The SYNTAX score was used to assess the severity of CAD; it was found to be statistically significantly higher in patients with metabolic syndrome than those without ($P = 0.001$).

Conclusion
Patients with metabolic syndrome have more severe CADs. Preventive measures against metabolic syndrome and its components are very important and could help avoid the large economic burden of secondary prevention.

Keywords:
coronary artery disease, metabolic syndrome, SYNTAX score

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Introduction

Epidemiology of coronary artery disease

The WHO reported in 2009 that coronary artery disease (CAD) is the leading cause of death worldwide, its incidence is increasing, and it has become a true pandemic. Nowadays, the burden of CAD is prevalent worldwide; the age-standardized death rates for CAD are decreasing in many developed countries, but are increasing in developing countries and transitional countries as a result of demographic changes, urbanization, and lifestyle changes [1].

The Egyptian National Hypertension Project and data from the WHO are the two principal sources of information on the epidemiology of CAD in the region. This nationally representative survey of 6733 individuals (about half were women) found an adjusted overall prevalence of CAD of 8.3%. The prevalence of CAD was higher in women (8.9%) relative to men (8%), but more clearly associated with an urban versus a rural location (8.8 vs. 7.2%) and age more than 50 years versus less than 50 years (11.1 vs. 5.1%) [2].

Metabolic syndrome represents a huge challenge to healthcare. Currently, it has assumed catastrophic proportions, but it poses an even greater threat in the future [3]. Although there are different criteria for the identification of metabolic syndrome, they all tend to agree that the core components are obesity (waist circumference), insulin resistance, dyslipidemia, and hypertension [4].

Definitions of metabolic syndrome: using the 2009 definition of the National Heart Lung and Blood Institute, the American Heart Association, the World

Heart Federation; the International Atherosclerosis Society, and the International Association for the study of obesity, metabolic syndrome is defined as the occurrence of three of a total of five abnormal findings, which are as follows:

(1) Elevated waist circumference (according to a population-specific and country-specific definition).
(2) Elevated triglycerides of at least 150 mg/dl (drug treatment for elevated triglycerides is an alternative indicator).
(3) Reduced high-density lipoprotein cholesterol (HDL-C) (drug treatment for reduced HDL-C is an alternative indicator) less than 40 mg/dl in men and less than 50 mg/dl in women.
(4) Elevated blood pressure (antihypertensive drug treatment in patients with a history of hypertension is an alternative indicator) systolic at least 130 and/or diastolic at least 85 mmHg.
(5) Elevated fasting glucose (drug treatment for elevated fasting glucose is an alternative indicator) at least 100 mg/dl [3].

Prevalence of metabolic syndrome in the Middle East: it was reported that in Egypt, other Arab, and Middle East countries, the thresholds of waist circumference diagnostic of abdominal obesity are derived from European data and a very high rate of obesity is reported among Egyptians; thus, there is a need to develop national guidelines for the definition of abdominal obesity. It was found that the cut-off points for waist circumference diagnostic of metabolic syndrome in Egyptian population were higher than those established in the guidelines (about 115 cm for men and 105 cm for women), and should be confirmed by further studies because the size of the waist circumference as an estimate of visceral obesity is still controversial subject [5].

A survey was conducted to estimate the prevalence of metabolic syndrome among children and adolescents in Egypt. The survey included 4250 adolescents (ranging in age from 10 to 18 years; males comprised 42.5% of the participants from seven governorates representing Egypt). The overall prevalence was significant among children and adolescents in Egypt; it was 7.4%, with no sex or area of residence predilection [6].

Pathophysiology of metabolic syndrome

Although obesity and insulin resistance remain at the core of the pathophysiology of metabolic syndrome, a number of other factors such as chronic stress and dysregulation of the hypothalamic–pituitary–adrenal axis, and autonomic nervous system increase in cellular oxidative stress, renin–angiotensin aldosterone system activity, and intrinsic tissue glucocorticoid actions as well as currently discovered molecules such as micro RNAs may also be involved in its pathogenesis [7].

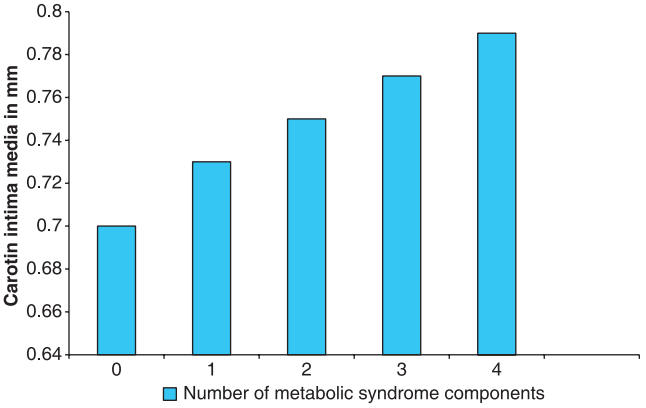
Risks of metabolic syndrome

Overall, a 1.5–3-fold higher risk of cardiovascular disease and coronary heart disease mortality has been found in several prospective studies, whereas a recent meta-analysis showed that metabolic syndrome was associated with a two-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality [8] (Fig. 1).

It was found that the presence of metabolic syndrome with and without diabetes is a strong independent determinant of early-onset CAD [10]. It was reported that of patients who fulfilled five metabolic syndrome criteria, 99% presented more than 20%coronary stenosis documented through angiography and 95% had a prevalence more than 50% [11].

In patients with myocardial infarction, metabolic syndrome and diabetes were highly prevalent and associated with an increased risk of death and cardiovascular events [11] Moreover, the presence of metabolic syndrome was shown to have an adverse impact on in-hospital morbidities (left ventricle failure, cardiogenic shock, and need for urgent revascularization), with a poorer prognosis among those with than those without metabolic syndrome presenting with acute coronary syndrome (ACS) independent of its association with diabetes and obesity [12].

Figure 1



Correlation between increasing number of metabolic syndrome components and carotid intima-media thickness [9].

Patients and methods

This work was carried out at Kasr Al Ainy Hospital at Cairo University and the Sohag Specialized cardiac and digestive system center to study the prevalence of metabolic syndrome among young patients presenting with acute coronary syndrome and its impact on the severity of coronary lesions as assessed by the SYNTAX score.

Patients were selected according to the following inclusion criteria:

(1) Age: between 18 and 45 years for men and between 18 and 55 years for women.
(2) Sex: both women and men were included.
(3) Acute coronary syndrome: patients presenting with acute coronary syndrome (STEMI, UA, NSTEMI) according to the 2007 American Heart Association definitions of myocardial infarction and UA/NSTEMI) [13].
(4) Willing to be participate in the study.

Exclusion criteria

(1) Age: younger than 18 years or older than 45 years for men and older than 55 years for women.
(2) Stable angina pectoris.
(3) Familial dyslipidemia.
(4) Evidence of vasculitis.

During the period of the study from January 2011 to January 2012, 122 patients who presented with ACS fulfilled our inclusion criteria; 85 were men (69.7%) and 37 were women (30.3%). The patients ranged in age between 27 and 55 years (age: mean ± SD (years) age 44.12 ± 5.56).

All patients were subjected to the following:

(1) Consent was obtained.
(2) Assessment of history and physical examination to obtain clinical data used for the diagnosis of metabolic syndrome (waist circumference according to clinical guidelines on identification, evaluation, and treatment of overweight and obesity in adults by the National institute of Health [14], systolic and diastolic blood pressure).
(3) Twelve-lead ECG.
(4) Laboratory investigations measurement of total cholesterol LDL, HDL levels, and blood sugar level as components of metabolic syndrome according to the 2009 statement of metabolic syndrome of the National Heart, Lung and Blood Institute [3].
(5) Assessment of metabolic syndrome and risk score: Using the 2009 definition of the National Heart Lung and Blood Institute; the American Heart Association; the World Heart Federation; the International Atherosclerosis Society; and International Association for the study of obesity, metabolic syndrome was defined as the occurrence of three of total of five abnormal findings [3].
(6) Diagnostic coronary angiography: to detect the severity of CAD according to SYNTAX score (Table 1) on the basis of the following components:
    (a) American Heart Association classification of the coronary tree segments [15].
    (b) Leaman score [16].
    (c) Total occlusion classification system [17].

Patients were classified into two groups according to the presence or absence of metabolic syndrome to determine the effect of metabolic syndrome on the severity of coronary lesions in comparison with nonmetabolic patients. The correlation was assessed between the number of metabolic risk components and severity of coronary lesions.

Results and statistical analysis

A two-sided p value < 0.05 was considered statistically significant and SPSS software (version 21, SPSS Inc, Chicago, IL, USA) was used for statistical analysis

(1) Numerical data are expressed as mean+SD.
(2) Comparison of changes in variables was performed using Student's *t*-test.

Table 1 SYNTAX score algorithm [18]

Dominance
Number of lesions
Segments involved per lesion
Lesion characteristics
Total occlusion
Number of segments involved
Age of the total occlusion (>3 months)
Blunt stump
Bridging collaterals
First segment beyond the occlusion visible by antegrade or retrograde filling
Side branch involvement
Trifurcation
Number of segments diseased
Bifurcation
Type
Angulations between the distal main vessel and the side branch <70°
Aorto-ostial lesion
Severe tortuosity
Length >20 mm
Heavy calcification
Thrombus
Diffuse disease/small vessels
Number of segments with diffuse disease/small vessels

(3) χ^2 was used to analyze non-numerical data.

The metabolic risk score was assessed; patients with a significant metabolic score of at least 3 risk score represented 66.4% of the total cohort (n = 81 patients) (Tables 2 and 3; Fig. 2).

Out of 81 patients with metabolic syndrome, 50 were men (61.7%) and 31 were women (38.3%). The mean age of the patients was 44.64 years, SD ± 5.59, with no statistically significant difference in age between metabolic and nonmetabolic syndrome patients (P = 0.148).

Out of 85 men in the study, 50 (58.82%) had metabolic syndrome whereas 31 of a total of 37 women in the study had metabolic syndrome (83.78%); thus, metabolic syndrome was more common in women than in men (P = 0.007).

Among patients with metabolic syndrome (n = 81), 42 (52%) had a score 4/5, 26 patients (32%) had a score 3/5, and 13 patients (16%) had a score 5/5 (Table 4).

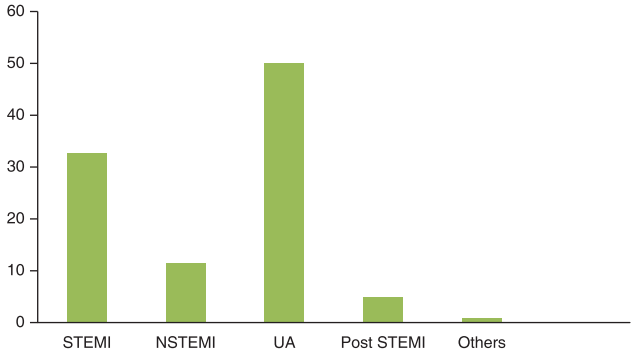
The most frequent metabolic risk in patients with metabolic syndrome was reduced HDL-C. Seventy-one patients (87.6%) had low HDL (P < 0.001), 54 patients (66.6%) had fasting blood glucose of at least 100 mg/dl (P < 0.001), 52 patients (64.1%) had elevated triglycerides (P < 0.001), 52 patients (64.1%) had blood pressure levels of at least 130 and/or diastolic at least 85 mmHg (P < 0.001), and 51 patients (62.9%) had increased waist circumference (P = 0.006) (Table 5).

There was no statistically significant difference in history relevant to CAD between patients with and without metabolic syndrome (P = 0.417) (e.g. prevalence of peripheral vascular disease, previous myocardial infarction, previous percutaneous coronary intervention, stable angina, previous stroke, coronary artery bypass graft surgery, and renal failure). The prevalence of hypertension was found to be significantly higher in metabolic syndrome patients (P = 0.007) (Table 6; Fig. 3).

The prevalence of diabetes was found to be significantly higher in metabolic syndrome patients (P = 0.001) (Table 7).

Smoking status was found to show no statistical significance in patients with metabolic syndrome

Figure 2



Type of acute coronary syndrome at the time of presentation.

Table 2 Distribution of risk factors for coronary artery disease in the study population

Risk factors	Number (% of total cohort)
Hypertension	53 (43.8)
Diabetes mellitus	46 (37.7)
Smoking	
Current	59 (48.4)
Former	13 (10.7)
Never	50 (41)
Dyslipidemia	33 (27)
Familial premature CAD	39 (32)

CAD, coronary artery disease.

Table 3 Types of acute coronary syndrome at presentation

Type of presentation	*n* (%)
STEMI	40 (32.79)
NSTEMI	14 (11.48)
UA	61 (50)
Post-STEMI angina	6 (4.92)
Others (early post-PCI unstable angina)	1 (0.82)
Total	122 (100)

Table 4 Frequency of metabolic risk score

Metabolic risk score	*n* (% of metabolic syndrome patients)
3/5	26 (32)
4/5	42 (52)
5/5	13 (16)

Table 5 Frequency of each metabolic component among metabolic syndrome patients

Metabolic risk	*n* (% of metabolic syndrome patients)
Low HDL	71 (87.6)
Increased fasting blood sugar	54 (66.6)
Elevated triglycerides	52 (64.1)
Blood pressure ≥130/85 mmHg	52 (64.1)
Increased waist circumference	51 (62.9)

HDL, high-density lipoprotein.

Table 6 Differences in the prevalence of hypertension between metabolic and nonmetabolic syndrome patients

HTN	Metabolic syndrome [*n* (%)]			χ^2	
	Negative	Positive	Total	χ^2	*P*-value
No	30 (73.17)	38 (47.50)	68 (56.20)	7.257	0.007
Yes	11 (26.83)	43 (52.50)	54 (43.85)		
Total	41 (100.00)	81 (100.0)	122 (100.00)		

HTN, hypertension.

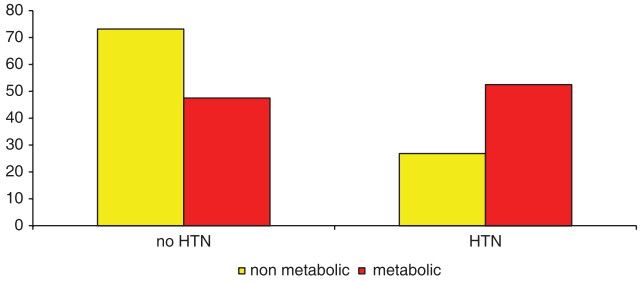
(P = 0.024). Moreover, patients with metabolic syndrome were found to have no statistically significant history of familial premature CAD (P = 0.091).

LDL cholesterol level showed no statistically significant difference in patients with metabolic syndrome and those without metabolic syndrome (P = 0.828). From the above data, a significant metabolic score can be considered as a risk factor for diabetes mellitus, systemic hypertension, and CAD in young patients irrespective of a high LDL level or smoking.

Patients with a significant metabolic risk presented more with unstable angina, less with STEMI, and showed a higher incidence of post infarction angina (Figs 4 and 5; Table 8).

Patients were subjected to coronary angiography. Significant CAD was found in all patients. The distribution of vessels affected was as follows (Table 9).

Figure 3



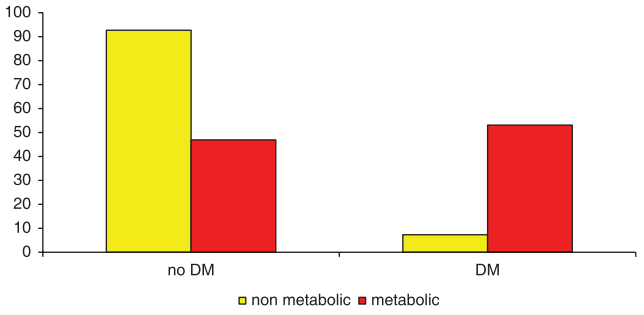
Hypertension in metabolic and nonmetabolic syndrome patients.

Patients with a significant metabolic risk score showed an increase in the frequency of left anterior descending lesions and no difference in the frequency of left main disease. Patients with metabolic syndrome had a significantly higher frequency of two-vessel disease and multivessel disease (Table 10).

A total of 38 patients had totally occluded vessels (31.2%) out of the total cohort; 27 patients had metabolic syndrome and the other 11 were not metabolic syndrome patients. Totally occluded vessels were found in 33.3% of metabolic syndrome patients and in 26.8% of nonmetabolic syndrome patients (P < 0.05).

The SYNTAX score was used to assess the severity of CAD; it was found to be statistically significantly higher in patients with metabolic syndrome than those without metabolic syndrome (P = 0.001) (Table 11; Fig. 6).

Figure 4



Prevalence of diabetes in metabolic and nonmetabolic syndrome patients.

Table 7 Differences in the prevalence of diabetes between metabolic and nonmetabolic syndrome patients

Diabetes mellitus	Metabolic syndrome [*n* (%)]			χ^2	
	Negative	Positive	Total	χ^2	*P*-value
Nondiabetic	38 (92.68)	38 (46.91)	76 (62.30)	24.278	<0.001
Diabetic	3 (7.32)	43 (53.09)	46 (37.7)		
Total	41 (100.00)	81 (100.0)	122 (100.00)		

Table 8 Type of presentation among patients with and without metabolic syndrome

Initial assessment	Metabolic syndrome [*n* (%)]			χ^2	
	Negative	Positive	Total	χ^2	*P*-value
STEMI	20 (48.78)	20 (24.69)	40 (32.79)	8.172	0.085
NSTEMI	3 (7.32)	11 (13.58)	14 (11.48)		
UA	17 (41.46)	44 (54.32)	61 (50.00)		
Post-STEMI	1 (2.44)	5 (6.17)	6 (4.92)		
Others	0 (0.0)	1 (1.23)	1 (0.82)		
Total	41 (100.00)	81 (100.00)	122 (100.00)		

Table 9 Distribution of vessels affected

Coronary artery affected	Left main (%)	Left anterior descending (%)	Left circumflex (%)	Right coronary artery (%)	Obtuse marginal (%)
Metabolic syndrome	7.4	50.6	6.2	22.2	8.6
Nonmetabolic syndrome	7.3	46.3	7.3	31.7	17

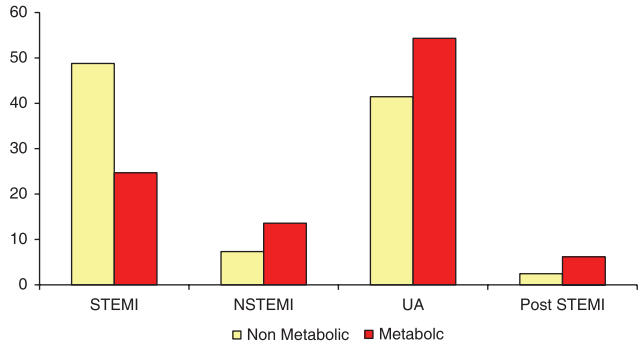
A positive correlation was found between increasing metabolic score and increasing severity of CAD according to the SYNTAX score ($P = 0.0049$).

Discussion

Cardiovacular diseases are main cause of death in developed and developing countries [19]. Metabolic syndrome patients have a higher risk of developing cardiovascular disease in general and CAD in particular [20]. The prevalence of metabolic syndrome is increasing alarmingly among adolescents and young adults because of adverse physical activity and dietary patterns [21].

We found that the prevalence of metabolic syndrome (identified according to the 2009 statement of metabolic syndrome by the National Heart, Lung and Blood Institute) among young patients presenting with acute coronary syndrome was high (66.39%). This was in agreement with other authors who reported a prevalence of 72% in patients with acute coronary syndrome [22]. Moreover, others reported a prevalence of 46% in patients presenting with ACS in six Middle Eastern arabian countries [23].

Figure 5



Relationship between the presence of metabolic syndrome and type of presentation.

Table 10 Number of vessels affected

Number of coronary arteries affected	Metabolic (%)	Nonmetabolic (%)
Single-vessel disease	37	70
Two-vessel disease	27	17
Multivessel disease	36	13

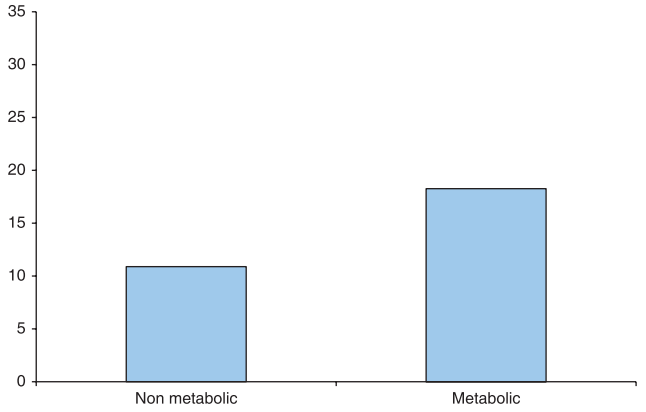
Young women with ACS showed a higher prevalence of metabolic syndrome than young men (83.78 vs. 58.82%) ($P = 0.007$). Studies have reported decreased survival in women with metabolic syndrome compared with women without metabolic syndrome [24].

In our study, smoking was found to be the most common risk factor (59% current and former smokers) present in young patients with CAD; it was more frequent in nonmetabolic syndrome patients. We found that reduced HDL, increasing fasting blood glucose, and increased triglycerides were the most common findings in young CAD patients with metabolic syndrome. This finding was in agreement with other studies that concluded that reduced HDL was the most effective lipid parameter affecting the severity of CAD [25].

Presentation with STEMI was more common among patients without metabolic syndrome than in those with metabolic syndrome (48.78 vs. 24.69%). Others more often found presentation with STEMI among young patients with metabolic syndrome [26]. In our study, the most frequeny presentation among young patients with metabolic syndrome was unstable angina.

A positive correlation was found between the presence of metabolic syndrome and SYNTAX score ($P = 0.001$). This was in agreement with others who found a positive correlation between the severity of CAD and the metabolic score [27].

Figure 6



Mean SYNTAX score in metabolic and nonmetabolic syndrome patients.

Table 11 SYNTAX score in metabolic and nonmetabolic syndrome patients

Metabolic syndrome	SYNTAX score		*t*-Test	
	Range	Mean ± SD	*t*	*P*-value
Negative	1.000–37.000	10.890 ± 8.991	–3.482	0.001
Positive	1.000–67.500	18.265 ± 11.947		

Recommendations

(1) Metabolic syndrome needs to be identified in Egyptian populations and should be treated with aggressive lifestyle modifications at a lower threshold for risk factors than in other populations.
(2) More studies are needed to identify factors that contribute toward the increased prevalence of metabolic syndrome in Egyptian populations, especially the young populaitons.
(3) More studies are needed to define metabolic syndrome in our community, especially racial and demographic criteria.

Conclusion

(1) The prevalence of metabolic syndrome is high in young Egyptian patients with CAD.
(2) Metabolic syndrome is a significant risk factor for CAD at a young age.
(3) Patients with metabolic syndrome have more severe CAD.
(4) Preventive measures against metabolic syndrome and its components are very important and could help avoid the large economic burden of secondary prevention.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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