

Prevalence of Metabolic Syndrome in Young Patients with ST-Elevation Myocardial Infarction

Tugba Kemaloglu Öz, Nazmiye Özbilgin¹, Aylin Sungur¹, Elif Gülsah Bas, Ahmet Zengin¹, Tayfun Gürol, Özer Soylu, Bahadır Dagdeviren

Department of Cardiology, Faculty of Medicine, Bahcesehir University, ¹Department of Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Center, Istanbul, Turkey

Abstract

Background: Atherosclerotic cardiovascular disease influences young patients as well as the elderly. A large proportion of patients with coronary artery disease (CAD) have metabolic syndrome (MS), although the frequency and association of its different components are not clear. To the best of our knowledge, there is no any study about the prevalence of MS among young patients with ST-elevation myocardial infarction (STEMI). We sought to determine the prevalence of MS in patients below 46 years of age who presented with STEMI and underwent primary percutaneous coronary intervention. **Methods:** In the present prospective study, 141 consecutive patients with STEMI <46 years of age admitted to intensive coronary care unit. STEMI was defined according to the ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. All patients were grouped presence of MS. In the second step, the components of MS were analyzed, excluding patients with diabetes mellitus (DM). **Results:** The total prevalence of MS was 46.8% ($n = 66$). In MS group, the most frequent component of MS was low high-density lipoprotein (HDL) levels (84.8%), followed by elevated triglycerides (TGs) (78.1%). A total of 121 patients did not have DM and 51 (42.1%) of these patients presented with MS. **Conclusions:** The prevalence of MS in young patients with STEMI is high. Low HDL cholesterol (HDLc) concentrations and high TG levels are cardiovascular risk factors, regardless of low-density lipoprotein cholesterol levels and they are found too often in our study. These results highlight the need to implement preventative strategies for reducing overall cardiovascular risk in young patients as well as elderly.

Keywords: Acute coronary syndrome, coronary artery disease, metabolic syndrome, ST-elevation myocardial infarction, young patients

INTRODUCTION

Metabolic syndrome (MS) is a clinical and biological entity of lipid and nonlipid factors of metabolic origin, which places subjects at risk for cardiovascular and cerebrovascular diseases. It has been previously defined by 3rd Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEPATP-III).^[1]

Worldwide, coronary artery disease (CAD) is the single most frequent cause of death.^[2] The atherosclerotic cardiovascular disease is a chronic disorder developing insidiously, and it remains as the major cause of premature death. Importantly, evidence revealing that increased cardiovascular risk starts to develop at a very young age has accumulated over the past decades.^[3] Acute myocardial infarction (AMI) among adults aged <46 is unusual, comprising 2%–10% of all cases.^[4]

Some studies have analyzed the prevalence of MS in patients with the acute coronary syndrome (ACS) but with mix populations

including both ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), also all age groups.^[5-7]

To the best of our knowledge, this is the first study to determine the prevalence of the MS in patients <46 years of age who presented with STEMI and underwent primary percutaneous coronary intervention (PCI).

METHODS

In the present prospective study, 141 consecutive patients with STEMI <45 years of age admitted to intensive coronary care unit. STEMI was defined according to the ESC guidelines

Address for correspondence: Dr. Tugba Kemaloglu Öz, Kadiköy, E5 Üzeri 23, Nisan Sok Merdivenköy No: 17, 34732 Kadiköy, Istanbul, Turkey.
E-mail: Tugbakemalogluoz@gmail.com.

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for the management of AMI in patients presenting with ST-segment elevation.^[8]

For the diagnosis of MS at baseline, we used the NCEP-ATP III criteria. MS was defined as having three or more of following criteria:^[1]

1. Abdominal obesity: Waist circumference (WC) >102 cm for men and >88 cm for women
2. Elevated Triglycerides (TGs) of ≥ 150 mg/dl
3. Low high-density lipoprotein (HDL) <40 mg/dl for men and <50 mg/dl for women
4. Elevated blood pressure $\geq 130/85$ mmHg
5. Elevated fasting blood glucose ≥ 110 mg/dl.

Patients who were not diagnosed with STEMI or had incomplete data or who used antilipidemic drugs were excluded from the study.

All patients underwent coronary angiography and results were analyzed. A coronary lesion was defined as significant if at least 70% of lumen diameter was reduced, except culprit lesion.

All patients were grouped first based on the presence of MS and then grouped again after excluding patients with diabetes mellitus (DM).

Demographic and clinical data were obtained from histories: age, sex, smoking, alcohol consumption, family history (premature coronary heart disease at 55 and 65 years of age in male and female first-degree relatives, respectively), and previous lipid-lowering treatment.

The diagnosis of DM was made by a fasting blood glucose level of 125 mg/dl or a history of DM, including those treated with diet control, oral medications, or insulin.

Blood pressure was determined in both arms after a 5-min rest. Patients were diagnosed with high blood pressure for an average (of 3 values) blood pressure during admission $\geq 130/85$ mm Hg or if a previous diagnosis of hypertension had been made and/or treatment had already been prescribed at the time of admission.

The heights and weights of all patients were taken before discharge. The weight in kilograms (kg) was measured using a calibrated scale with capacity for 180 kg and increments of 100 g. The height, in meters, was measured using anthropometric scale. The body-mass index (BMI) was calculated using the formula: Body weight (kg)/height² (m²). We used the international classes of BMI: Obesity (BMI ≥ 30 kg/m²), overweight (BMI 25–29.9 kg/m²), normal (BMI 18.5–24.9 kg/m²), and underweight (BMI <18.5 kg/m²).

Waist and hip circumferences (HC) were recorded. WCs were measured at the level midway between the lowest rib and the iliac crest, the thinnest part of abdomen and HC were measured at the maximum circumference between the hips and buttocks.

Plasma samples were obtained after at least 12 h of fasting. Total cholesterol and TG levels were measured

using an automated enzyme analyzer, and low-density lipoprotein (LDL) concentrations were calculated using the Friedewald formula whenever plasma TG concentrations were <400 mg/dl (Advia Systems, Siemens, Australia). D-dimer was estimated using automatic latex immunoassay (HemosIL™, Instrumentation Laboratory, USA). Fibrinogen-C was measured according to the method of Class (HemosIL^R, Instrumentation Laboratory, USA). C-reactive protein was measured using latex-enhanced immunotubidimetry (Advia System, Siemens, Australia).

Transthoracic echocardiography was performed in all patients before discharge.

Quantitative variables were expressed as a mean \pm standard deviation, median (interquartile range) and qualitative variables as absolute and relative frequencies. Normally distributed data were analyzed using the Student's *t*-test to compare means; otherwise, the Mann–Whitney U-test (MWU) was used. The Chi-square test was used to analyze differences between qualitative variables. A two-sided $P < 0.05$ was used as a cut-off for statistical significance. Results of χ^2 test were expressed as Chi-square (degrees of freedom, sample size) = Pearson's Chi-square value, *P* value. Results of Student's *t*-test were expressed as *t* (degrees of freedom) = *t* value, *P* value, 95% confidence interval (CI). Results of MWU-test were expressed as MWU value, *P* value. The SPSS software version 17.0 (SPSS science, Chicago, IL, USA) was used for statistical analyses.

Institutional Review Board approved this study for research, and all patients gave written informed consent before the study.

RESULTS

The present study included a total of 141 consecutive patients with STEMI. The majority of the admitted patients were men (87.9%), and the mean age was 38.3 ± 4.6 , ranging from 26 to 45 years. Table 1 shows the demographic and clinical characteristics of the patients stratified by MS status, and we compared the baseline characteristics of patients with and without MS. BMI was significantly higher in the MS group ($\chi^2 [2, 139] = 19.17, P < 0.001$). Waist and HC were also significantly higher in the MS group ($t [138] = -4.24, P < 0.001, 95\% \text{ CI} [-10.39, -3.79]$ and $t [138] = -3.24, P < 0.001, 95\% \text{ CI} [-6.91, -1.67]$; respectively). Systolic and diastolic blood pressures were significantly elevated in the MS group ($t [137] = -3.61, P < 0.001, 95\% \text{ CI} [-14.78, -4.33]$ and $t [137] = -3.78, P < 0.001, 95\% \text{ CI} [-9.57, -2.99]$; respectively). Fasting plasma glucose was significantly higher in the MS group; $t (138) = -3.92, P < 0.001, 95\% \text{ CI} (-46.26, -15.23)$. Total cholesterol and TG showed significantly higher levels in the MS group ($t [138] = -2.23, P = 0.02, 95\% \text{ CI} [-27.88, -1.66]$ and $t [136] = -6.19, P < 0.001, 95\% \text{ CI} [-147.08, -75.87]$, respectively). Fibrinogen was also found to be significantly higher in the patients with MS; $t (128) = -2.17, P = 0.01, 95\% \text{ CI} (-69.49, -3.3)$. However, HDL cholesterol (HDLc) and LDL cholesterol (LDLc) levels did not significantly differ between the groups.

Table 1 Demographic and clinical characteristics of the patients stratified by metabolic syndrome status

| Variable | MS | | P |
|---------------------------------|---------------------------|---------------------------|--------|
| | Positive (n=66: 46.8%) | Negative (n=75: 53.2%) | |
| Age (years) | 39.0±4.0 | 37.7±5.1 | 0.12 |
| Men, n (%) | 55 (83.3) | 69 (92.0) | 0.11 |
| Smoker, n (%) | 55 (83.3) | 64 (85.3) | 0.74 |
| Alcohol consumer, n (%) | 12 (18.2) | 6 (8.1) | 0.07 |
| Drug abuser, n (%) | 1 (1.5) | 1 (1.3) | 0.95 |
| Family history, n (%) | 21 (31.8) | 18 (24.0) | 0.30 |
| BMI (kg/m ²), n (%) | 29.3±4.1 | 26.4±3.6 | |
| <25 | 11 (16.7) | 28 (37.3) | <0.001 |
| 25-29.9 | 22 (34.8) | 36 (48.0) | |
| >30 | 32 (49.2) | 11 (14.7) | |
| Waist circumference (cm) | 98.4±11.3 | 91.5±8.3 | <0.001 |
| Hip circumference (cm) | 105.3±8.5 | 101.1±7.1 | <0.001 |
| Blood pressure (mmHg) | | | |
| Systolic | 128.2±17.4 | 118.6±13.5 | <0.001 |
| Diastolic | 78.2±11.4 | 72.0±7.9 | <0.001 |
| Fasting plasma glucose (mg/dl)* | 47 (113) | 14.2 (94) | <0.001 |
| Total cholesterol (mg/dl) | 196.5±39.8 | 181.7±38.5 | 0.02 |
| LDL-C (mg/dl) | 117.7±31.5 | 121.7±36.1 | 0.50 |
| HDL-C (mg/dl) | 35.1±11.8 | 35.1±9.0 | 0.99 |
| Triglycerides (mg/dl)* | 107 (190) | 62.2 (110) | <0.001 |
| CRP (mg/dl)* | 3.4 (4.2) | 1.0 (3.4) | 0.15 |
| Fibrinogen (mg/dl) | 389.3±110.5 | 348.3±78.9 | 0.01 |
| D-dimer (ng/ml)* | 136.0 (123.0) | 135.2 (117.5) | 0.52 |
| Ejection fraction (%) | 51.7±8.6 | 52.5±9.1 | 0.60 |

*Values expressed as median (interquartile range). Values are mean±SD or n (%). BMI: Body mass index, CRP: C-reactive protein, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, MS: Metabolic syndrome, SD: Standard deviation

The total prevalence of MS using ATPIII criteria was 46.8% (n = 66). In MS group, the most frequent component of MS was low HDL level (84.8%), followed by elevated TG (78.1%), elevated blood pressure (63.6%), carbohydrate metabolism disorder (59.1%) and in the last place, abdominal obesity (46.%) [Figure 1]. We found no MS components in 11 patients (7.8%). 15 patients with MS (22.7%) had DM.

In total, MS was not found in 75 (53.2%) patients. The most frequent component was among the patients without MS was low HDLc level (67.6%), followed by elevated blood pressure (25.7%), elevated TG (23.0%), carbohydrate metabolism disorder (21.3%), and abdominal obesity (8.0%). Five patients without MS (6.7%) had DM.

In this study, 121 patients did not have DM and 51 (42.1%) of these patients presented with MS [Table 2]. The most prevalent component of MS was low HDLc (73.6%), followed by elevated TG (45.5%), elevated blood pressure (43.0%), carbohydrate metabolism disorder (30.6%) and, finally, abdominal obesity (23.1%) [Figure 1]. In this substudy prevalence of alcohol consumption was significantly higher in patients with MS than patients without MS;

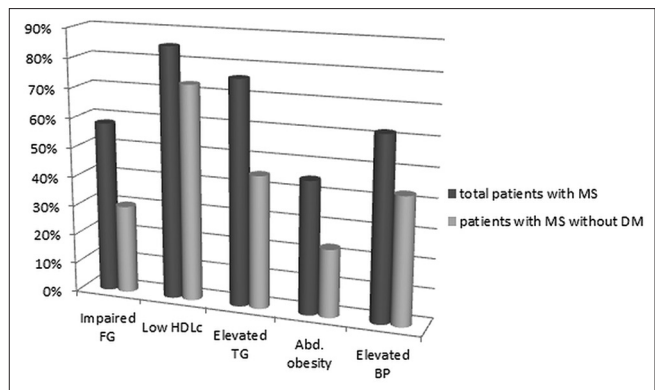


Figure 1: Distribution of metabolic syndrome criterias in all patients with metabolic syndrome and after excluding patients with DM. Abd: Abdominal, BP: Blood pressure, DM: Diabetes mellitus, FG: Fasting glucose, HDLc: High-density lipoprotein cholesterol, TG: Triglycerides

$\chi^2 (1, 120) = 4.09, P = 0.04$. BMI was higher in the MS group; $\chi^2 (2,120) = 15.33, P < 0.001$. Waist and HC were also significantly higher in patients with MS ($t [119] = -3.53, P < 0.001, 95\% \text{ CI } [-10.24, -2.88]$ and $t [119] = -2.57, P = 0.01, 95\% \text{ CI } [-6.83, -0.88]$, respectively). Systolic and diastolic blood pressures were significantly elevated in the MS group ($t [118] = -3.94, P < 0.001, 95\% \text{ CI } [-15.76, -5.21]$ and $t [118] = -3.72, P < 0.001, 95\% \text{ CI } [-10.05, -3.07]$; respectively). Fasting plasma glucose was significantly higher in the MS group (MWU = 1046, $P < 0.001$). Total cholesterol showed significantly higher levels in patients with MS; $t (118) = -2.03, P = 0.04, 95\% \text{ CI } (-28.78, -0.36)$. TG levels was significantly higher in the MS group (MWU = 636.5, $P < 0.001$). Fibrinogen was also found to be significantly higher in the patients with MS; $t (109) = -3.01, P < 0.001, 95\% \text{ CI } (-84.97, -17.49)$.

When we assessed the most prevalent combination of ATPIII factors in the patients with MS, 12 patients (18.2%) fulfilled the triad of low HDLc levels, elevated TG and carbohydrate metabolism disorder. The most prevalent tetrad was (n = 9, 13.6%) low HDLc levels, elevated TG, carbohydrate metabolism disorder and elevated blood pressure. In the patients without DM the most prevalent triad of MS was low HDLc levels, elevated TG and elevated blood pressure (n = 10, 19.6%). The most prevalent tetrad was found same in two groups.

Single-vessel involvement with left anterior descending artery (LAD), as the culprit lesion, was the most frequent presentation and followed by the circumflex artery and right coronary artery. Distribution of vascular lesions in patients with MS was compared to patients without MS, and no significant difference was observed among the groups.

DISCUSSION

In the present prospective study, 141 consecutive patients with STEMI < 45 years of age who were treated with primary PCI were evaluated. Only a few studies have evaluated the prevalence of MS, as defined by the nonmodified NCEP-ATP

Table 2: Demographic and clinical characteristics of the patients stratified by metabolic syndrome status, after excluding patients with diabetes mellitus

| Variable | MS | | P |
|---------------------------------|---------------------------|---------------------------|--------|
| | Positive (n=51: 42.1%) | Negative (n=70: 57.9%) | |
| Age (years) | 38.3±4.1 | 37.4±5.0 | 0.35 |
| Men, n (%) | 41 (80.4) | 64 (91.4) | 0.61 |
| Alcohol consumer, n (%) | 10 (19.6) | 5 (7.2) | 0.04 |
| Drug abuser, n (%) | 1 (2.0) | 1 (1.4) | 0.82 |
| Family history, n (%) | 16 (31.4) | 17 (24.3) | 0.38 |
| BMI (kg/m ²), n (%) | 28.9±4.0 | 26.3±3.6 | |
| <25 | 10 (20.0) | 28 (40.0) | <0.001 |
| 25-29.9 | 17 (34.0) | 32 (45.7) | |
| >30 | 23 (46.0) | 10 (14.3) | |
| Waist circumference (cm) | 97.7±12.0 | 91.1±8.4 | <0.001 |
| Hip circumference (cm) | 105.0±9.1 | 101.2±7.3 | 0.01 |
| Blood pressure (mmHg) | | | |
| Systolic | 128.5±16.3 | 118.0±12.8 | <0.001 |
| Diastolic | 78.4±11.2 | 71.8±8.0 | <0.001 |
| Fasting plasma glucose (mg/dl)* | 24.0 (110.0) | 22.2 (97.5) | <0.001 |
| Total cholesterol (mg/dl) | 196.5±40.2 | 181.9±37.8 | 0.04 |
| LDL-C (mg/dl) | 118.0±32.2 | 122.0±36.0 | 0.53 |
| HDL-C (mg/dl)* | 9.0 (36.0) | 13.0 (34.5) | 0.52 |
| Triglycerides (mg/dl)* | 103.5 (190.0) | 89.7 (140.0) | <0.001 |
| hsCRP (mg/dl)* | 3.5 (2.1) | 3.8 (1.5) | 0.22 |
| Fibrinogen (mg/dl) | 401.4±100.3 | 350.2±78.9 | <0.001 |
| D-dimer (ng/ml)* | 106.0 (110.0) | 119.0 (115.5) | 0.59 |
| Ejection fraction (%) | 51.7±8.5 | 52.9±8.6 | 0.50 |

*Values expressed as median (interquartile range). Values are mean±SD or n (%). BMI: Body mass index, CRP: C-reactive protein, DM: Diabetes mellitus, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, SD: Standard deviation, MS: Metabolic syndrome

III criteria and to the best of our knowledge, there is not any study about the prevalence of MS among young patients with STEMI.

The present study found that patients with STEMI had a high prevalence of MS (46.8%). In two previous studies, patients aged <45 years with STEMI or NSTEMI were evaluated, and the prevalence of MS was 40.4%^[9] and 46.0%^[10] In a previous Turkish study, 217 patients (mean age at baseline 49.1 ± 13 years) with CAD, the prevalence of MS was reported 53%.^[11] The other studies reported the prevalence of MS in ACS 29%–66%.^[5,6,12-14] In a cross-sectional study, prevalence of MS was found 49.7% among adult patients who admitted to cardiology department.^[14] In another study, 1255 patients aged 65 years old and over without any acute illness were evaluated, and prevalence of MS was reported 23.8%.^[15]

When the twenty patients with DM were excluded, 51 of the remaining 121 (42.1%) have >3 criteria for MS. The other studies found the prevalence of MS among the patients with ACS without DM, 34%^[5] and 42%.^[10]

The average value for criteria of MS (TG, systolic and diastolic blood pressure, fasting plasma glucose, and WC) were all significantly higher in patients with MS compared with those without but no significant difference was observed between two groups for HDLc and LDLc levels. Multiple epidemiological studies have demonstrated that HDLc concentrations are inversely and independently associated with the development of ischemic heart disease,^[2] and hence, in our study prevalence of low HDLc level was seen very common in all groups. Statistical significance between patients with and without MS was maintained even when patients with known or newly diagnosed DM excluded. At the same time, low HDLc level was most frequent component of MS, followed by elevated TG [Figure 1]. The ATPIII concluded that low HDLc concentrations and high TG levels are cardiovascular risk factors, regardless of LDLc levels.^[1] And, they are found very common in young patients with STEMI, but the first target is LDLc level according to current guidelines in all ages.^[2,16]

The most frequent triad combination of MS was impaired glucose tolerance, low HDLc level and elevated TG in the MS group without excluding DM. In a retrospective study of 574 patients with ACS, low HDLc, elevated blood pressure and impaired glucose tolerance were found to be the most frequent triad of MS.^[5]

Perez *et al.* reported that fibrinogen and C-reactive protein (CRP) levels were significantly higher in adults with MS than without MS.^[17] Differently, in this study fibrinogen levels were found significantly higher in patients with MS and there was no significant difference between two groups in the level of CRP and D-dimer. But, in our study, all patients with STEMI and CRP and D-dimer levels could be increased due to STEMI in both groups. In a case–control study, 220 patients with ACS were compared with 116 healthy volunteers, and ACS cases showed 4-fold higher median CRP concentration on admission than healthy controls.^[18] However, the d-dimer level was found to be higher among patients with ACS.^[19-24] In another previous study, 2722 nondiabetic men aged 60–79 years with no history of CAD were determined, and insulin resistance was found significantly associated with increased CRP, but the association with fibrinogen and fibrin d-dimer were found weak.^[25]

Among our patients, single-vessel involvement with LAD was the most frequent culprit lesion within both groups. Colkesen *et al.* reported characteristics of STEMI in young patients aged <35. They reported that young patients with acute STEMI showed a preponderance of single-vessel disease and acute anterior STEMI owing to occluded LAD artery.^[26]

In our study, there was no relationship between MS and the number of vessels affected. However, Marso *et al.* determined plaque composition of 673 patients with ACS and lesion length, plaque burden, necrotic core, and calcium content were significantly greater among nonculprit lesions of patients with diabetes or MS.^[27] Furthermore, Yoon *et al.* found relationship between MS score and severity of coronary atherosclerosis.^[28]

In both studies, the assessment of vessels was different and more detailed than our study.

Another study included 100 patients with STEMI, and 40% of these patients have MS based on Consensus statement for diagnosis of MS for Asian Indians, 49% had anterior wall MI and 37% had inferior wall MI.^[29] In the different data that study population consisted of 467 men admitted with ACS. A total of 324 (69.37%) patients fulfilled the criteria stated in the latest joint statement for the definition of MS.^[8] Among them, STEMI was present in 178 (54.9%) patients and NSTEMI-ACS in 146 (45.1%) patients (*P* value, nonsignificant). There was also no significant difference in the prevalence of different types of ACS between the MS and non-MS groups (STEMI, 54.9% vs. 51.7%; NSTEMI-ACS, 45.1% vs. 48.3%, respectively; *P* = 0.294 for both).^[30]

CONCLUSIONS

This study revealed that the prevalence of MS in young patients with STEMI is high. Moreover, the most common criteria of MS are low HDLc and followed by elevated TG. Finally, the prevalence of MS is increasing worldwide, and it influences all age groups, and hence, these results highlight the need to implement preventative strategies for reducing overall cardiovascular risks in young patients as well as elderly.

Limitations

The study had several limitations. First, this is a single-center study. Moreover, second, unfortunately, we could not sought to examine the long-term clinical outcomes of all patients. Moreover, third, in our study, the assessment of vessels lesions was not detailed in both groups.

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Conflicts of interest

There are no conflicts of interest.

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