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Original Article

Predictors of multivessel involvement in patients under 40 years of age receiving primary PTCA for STEMI

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Abstract

Aim: The angiographic features of myocardial infarction in young patients and the factors affecting these features differ from those in elderly patients and have not been fully established. The aim of this study was to investigate the factors involved in the development of multivessel disease in patients aged 40 years or younger with ST-segment elevation myocardial infarction (STEMI).

Material and Methods: A total of 148 patients aged 40 years or younger who underwent primary percutaneoustransluminal coronary angioplasty for STEMI were included in the study. The demographic features, angiographic features, biochemical data and risk factors of the patients were reviewed retrospectively.

Results: Assessment of the risk factors showed that 91.2% of the patients were male, 73% were smokers, 56.8% were hyperlipidemic, 36.1% were hypertensive and 23.1% had diabetes mellitus. A positive family history was present in 31.1% of the patients. Hyperlipidemia was significantly more common (p=0.008) and the hemoglobin values were significantly lower (p<0.001) in the patients with multivessel disease than those with single-vessel disease. Anemia was also significantly more prevalent in the patients with multivessel disease (p<0.001).A multivariate regression analysis showed that anemia was associated with a 21.740-fold increase(95% CI: 2.921-161.817; p=0.003)in the likelihood of developing multivessel disease, irrespective of other risk factors, while hyperlipidemia was associated with a 3.742-fold increase (95% CI: 1.104-12.679; p=0.034) and male sex was associated with a 9.390-fold increase (95% CI: 1.019-86.570) (p=0.048).

Conclusion: Anemia, hyperlipidemia and male sex are associated with multivessel disease in STEMI patients aged 40 years or younger.

Keywords: Anemia;hyperlipidemia; multivessel; young myocardial infarction.

INTRODUCTION

Ischemic heart disease remains the most common cause of mortality and morbidity in the world.(1)The proportion of STEMI in acute coronary syndromes (ACS) has decreased over time (2).

Although the long-term prognosis of STEMI patients has improved, this improvement is mostly seen in a subset of patients undergoing primary angioplasty (3). STEMI in patients younger than 40 years of age represents approximately 8% of all STEMI cases. The clinical and angiographic features of ACS in patients of a young age differ from those in elderly patients(4). STEMI at a younger age is usually associated with angiographic findings characterized by single-vessel involvement and less complicated coronary lesions (5,6). Previous studies have shown that younger MI patients are more likely to smoke, have lower high-density lipoprotein (HDL) levels and to be of male sex in comparison to elderly MI patients (7). In this group of patients, acute coronary thrombosis may play a fundamental role in the pathophysiology of the disease. However, approximately one third of these patients have multivessel involvement and more complex coronary lesions. Coronary atherosclerosis may be considered chronic and more common in these patients. In this study, we aimed to examine the angiographic and demographic characteristics of younger patients who had undergone primarypercutaneous transluminal coronary angioplasty

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(PTCA) for STEMI and to investigate the differences between the patients with multivessel coronary artery disease(CAD) and those with single-vessel CAD angiographically.

MATERIAL and METHODS

Patient Selection

Patients aged 40 years or younger who underwent PTCA following a diagnosis of STEMI at our clinic between 2014 and 2017 were included in the study. Patients with prior percutaneous coronary intervention, chronic kidney failure, malignancies and known autoimmune diseases, as well as pregnant women, were excluded from the study. The final study sample comprised 148 patients. The study protocol was reviewed and approved by the institutional ethics committee in accordance with the Declaration of Helsinki.

Collection of Patient Data

Complete blood count and biochemical data at presentation were reviewed retrospectively for all the patients. The cardiac risk factors of the patients, including hypertension, diabetes mellitus, hyperlipidemia, family history and smoking status, were recorded. Smoking status was defined as a current smoking habit or a history of smoking. Hyperlipidemia was defined as the prior use of statin therapy for elevated cholesterol levels, a fasting low-density lipoprotein (LDL) cholesterol greater than 130 mg/dl or a total cholesterol greater than 200 mg/dl. Hypertension was defined as a prior diagnosis of hypertension,a history of antihypertensive medication use or blood pressure values above antidiabetic drugs or insulin, a fasting blood glucose above 126 mg/dl and a postprandial blood glucose above 200 mg/dl or an HbA1c greater than 6.5%. A positive family history was defined as first-degree relatives younger than 55 years of age for males and younger than 65 years for femaleswho underwent coronary PCI or a coronary artery bypass graft or suffered a myocardial infarction. Anemia was defined as an Hb value less than 13g/dl for males and less than 12g/dl for female patients. The angiographic features and the presence of single- or multivessel CAD among the patients were also examined.Single-vessel CAD was considered when there was >50% stenosis in one of the coronary arteries, and multivessel CAD was diagnosed in the case of >50% stenosis in multiple coronary arteries.

Statistical Analyses

The Kolmogorov–Smirnov test was used to analyse whether the continuous numerical variableswere normally distributed, and the homogeneity of variance was assessed using Levene's test. The descriptive statistics were presentedas mean ± standard deviation for the continuous numerical variables or median (the width of the interquartile ranges), and the categorical variables were expressed as the number of cases and percentages (%).

The significance of the mean between-group differences was assessed using the Student's t-test, and the Mann–Whitney U test was used to analyze the significance of the difference in the continuous numerical variables when the assumptions for the parametric test statistics were not met. The categorical variables were assessed using Fisher's exact probability test when the expected frequency in at least one of the cells in the 2x2 contingency tables was less than 5, and the chi-square test corrected for continuity was used when the expected frequency was between 5 and 25. Pearson's chi-square test was used in all other cases.

The concurrent effects of all the potential risk factors used for determining the single- and multivessel CAD subgroups within the STEMI group were assessed with the multivariable logistic regression analysis using a prospective likelihood ratio methodology. All the variables with a p value of <0.10 in the univariate statistical analyses were included in the logistic regression model as candidate risk factors. Additionally, the odds ratios and 95% confidence intervals were estimated for each variable.

The data analyses were performed using the IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY) software package. Unless indicated otherwise, all the values with a p value less than 0.05 were considered statistically significant. However, Bonferroni's correction was applied to control Type I error rates in all the multiple comparisons.

RESULTS

Evaluation of the clinical, demographic and biochemical data of the study patients

The clinical, demographic and biochemical data of the study sample are summarized in Table 1.A total of 148 patients were included in the study.Of these, 91.2% were male, 36.1% were hypertensive,23.1% were diabetic, 56.8%were hyperlipidemic and 73% were smokers. A positive family history was present in 31.1% of the patients. Nearly all the patients had at least one risk factor (Figure 1). Low mean HDL values (31 mg/dl) were also detected.

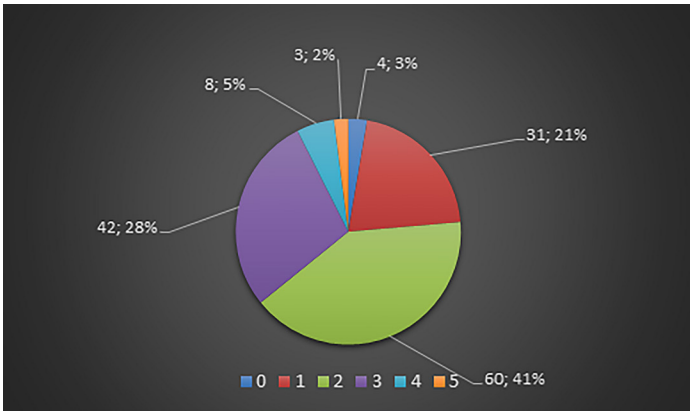

Figure 1. Percentage and number of risk factors

Table 1. General characteristics of the STEMI patients	
Age (years)	36.3±3.9
Sex	
Male	135 (91.2%)
Female	13 (8.8%)
HT	53 (36.1%)
DM	34 (23.1%)
HL	83 (56.8%)
Smoking	108 (73.0%)
Family history	46 (31.3%)
Number of vessels involved	
Single	102 (68.9%)
Multiple	46 (31.1%)
HGB (g/dl)	14.63±1.84
Anaemia	16 (11.1%)
WBC (103/mm3)	11.99 (4.25)
PLT (103/mm3)	261.00 (94.2)
MPV (fl)	8.58 (1.80)
RDW (%)	11.39 (1.70)
PCT (%)	0.21 (0.08)
PDW (%)	16.60 (4.08)
NEU (103/mm3)	8.37 (4.29)
LYM (103/mm3)	2.51 (1.28)
NLR	3.14 (2.75)
LDL-C (mg/dl)	123.00 (55.5)
HDL-C (mg/dl)	31.00 (11.00)
TRIG (mg/dl)	164.00 (192)
Creatinine (mg/dl)	0.80 (0.20)
AST (IU/L)	61.50 (89.75)
ALT (IU/L)	34.00 (30.25)
Bilirubin (mg/dl)	0.22 (0.15)
Glucose (mg/dl)	119.00 (65.50)
Uric Acid (mg/dl)	5.45±1.50

HT: hypertension; DM: diabetes mellitus; HL: hyperlipidaemia; HGB: haemoglobin; WBC: white blood cell; PLT: platelet; MPV: mean platelet volume; RDW: red cell distribution width; PCT: platecrit; PDW: platelet distribution width; NEU: neutrophil; LYM: lymphocyte; NLR: neutrophil lymphocyte ratio; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TRIG: triglyceride; AST: aspartat aminotransferase; ALT: alanin aminotransferase

Evaluation of the angiographic features of the study patients

The angiographic features of the patients are summarized in Table 2.Based on the angiographic findings, single-vessel CAD was detected in 68.1% of the patients and multivessel CAD in 31.9%. Among the patients with multivessel CAD, three coronary vessels were involved in one third and two coronary vessels in two thirds of the patients.Among the patients with single-vessel CAD, 62.7% had involvement of the LAD, 23.5% had right coronary artery (RCA) involvement and Cx involvement was present in 13.8%.

Comparison of the single- and multivessel CAD patients

The study patients were divided into two subgroups according to vessel involvement: (1) the single-vessel CAD, (2) the multivessel CAD. The clinical and biochemical properties of each group are summarized in Table3.A significantly greater rate of hyperlipidaemia was found among the multivessel CAD patients (p=0.0008).A comparison of the blood parameters between the groups showed lower hemoglobin levels in the multivessel CAD patients(p<0.0001).Anemia was also more common in the multivessel CAD patients based on an anaemia definition of an Hb below 13 g/dl for males and below 12 g/dl for females (p<0.0001).A multiple regression analysis showed that multivessel CAD was 21.740 times more likely to occur in patients with anemia than patients without anemia(95% CI: 2.921–161.817; p=0.003), and hyperlipidemia was associated with a 3.742-fold increased risk for the development of multivessel CAD(95% CI: 1.104–12.679; p=0.034), irrespective of other risk factors. Additionally, male sex was associated with a statistically significantly greater risk of multivessel CAD after adjustment for other risk factors than female sex (OR=9.390, 95% CI: 1.019–86.570; p=0.048) (Table 4). Both groups had comparable rates of diabetes mellitus,hypertension and family history.

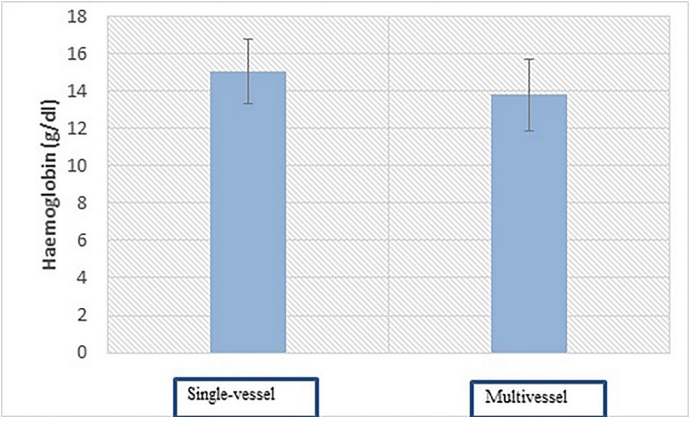

Figure 2. Comparison of the hemoglobin levels between the single- and multivessel groups

Table 2. Demographic, clinical and biochemical data of STEMI patients stratified into two groups by the number of vessels involved

	Single-vessel CAD(n=102)	Multivessel CAD (n=46)	p-value
Age (years)	36.2±3.8	36.5±4.0	0.702
Sex			0.065
Male	90 (88.2%)	45 (97.8%)	
Female	12 (11.8%)	1 (2.2%)	
HT	34 (33.7%)	19 (41.3%)	0.478
DM	22 (21.8%)	12 (26.1%)	0.717
HL	49 (49.0%)	34 (73.9%)	0.008
Smoking	78 (74.5%)	30 (65.2%)	0.456
Family history	34 (33.7%)	12 (26.1%)	0.467
HGB (g/dl)	15.03±1.70	13.77±1.88	<0.001
Anaemia	6 (6.1%)	10 (22.2%)	0.010
WBC (103/mm3)	11.72 (4.82)	12.18 (3.83)	0.679
PLT (x103/mm3)	259.00 (89.00)	268.00 (120.50)	0.532
MPV (fl)	8.50 (1.51)	8.60 (2.45)	0.789
RDW (%)	11.30 (1.40)	11.84 (2.33)	0.067
PCT (%)	0.21 (0.07)	0.20 (0.10)	0.611
PDW (%)	16.60 (4.09)	16.60 (3.96)	0.921
NEU (103/mm3)	8.28 (4.81)	8.40 (3.52)	0.738
LYM (103/mm3)	2.51 (1.32)	2.62 (1.19)	0.755
NLR	3.04 (3.08)	3.25 (2.09)	0.568
LDL-C (mg/dl)	109.00 (47.50)	134.00 (62.50)	0.079
HDL-C (mg/dl)	32.00 (13.00)	29.00 (10.00)	0.082
TRIG (mg/dl)	186.00 (197.00)	154.00 (183.00)	0.854
Creatinine(mg/dl)	0.80 (0.22)	0.80 (0.18)	0.745
AST (IU/L)	54.50 (94.00)	70.50 (128.50)	0.187
ALT (IU/L)	33.50 (30.50)	34.50 (30.75)	0.483
Bilirubin (mg/dl)	0.22 (0.15)	0.21 (0.17)	0.510
Glucose(mg/dl)	116.50 (67.00)	126.00 (70.65)	0.108
Uric Acid(mg/dl)	5.49±1.47	5.37±1.57	0.695

HT: hypertension; DM: diabetes mellitus; HL:hyperlipidaemia; HGB:haemoglobin; WBC: white blood cell; PLT: platelet; MPV: mean platelet volume; RDW: red cell distribution width; PCT: platecrit;PDW: platelet distribution width; NEU: neutrophil; LYM: lymphocyte; NLR: neutrophil lymphocyte ratio; LDL-C:low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol;TRIG: triglyceride; AST:aspartat aminotransferase; ALT: alanin aminotransferase

Table 3. Factors playing a major role in differentiating the patients with single-vessel disease from those with multivessel disease in the STEMI group

	OR	95% CI	p-value
Male gender	9.390	1.019–86.570	0.048
Hyperlipidaemia	3.742	1.104–12.679	0.034
Anaemia	21.740	2.921–161.817	0.003

OR: odds ratio; CI: confidence interval

Table 4. Distribution of coronary artery disease in the patients with single- andmultivessel disease

Group	Total no. of patients	LAD [no. (%) of pts]	RCA [no. (%) of pts]	CX [no. (%) of pts]
Single-vessel disease	102 (68.1)	64 (62.7)	24 (23.5)	14 (13.8)
Two-vessel disease	31 (21)	25 (80)	21 (67)	16 (51.6)
Three-vessel disease	15 (10.9)	15 (100)	15 (100)	15 (100)

OR: odds ratio; CI: confidence interval

DISCUSSION

It has been suggested that ACS have a better short-term prognosis among younger patients (7). While the incidence of STEMI is lower among young people, it is still common. ACS in young people arecharacterized by single-vessel involvement where thrombosis is the predominant pathophysiology. Nevertheless, about one-third of patients have multivessel disease (5,6). Previous studies have shown that the majority of patients have at least one risk factor for CAD (8). In the current study, nearly all the patients had at least one risk factor.The risk factors for CAD may vary depending on age.In the literature, male sex, smoking and dyslipidemiacharacterised by low HDL have been reported to be more common in younger MI sufferers (9-11). This is consistent with our results.Diabetes mellitus is considered to be a CAD risk factor equivalent to that of the normal population but is recognized as a major risk factor for multivessel disease (12). However,in our study sample, diabetes mellitus had a comparable prevalence between the patients with single-vessel CAD and those with multivessel CAD. There was also no difference in hypertension prevalence between the two groups. In contrast to our findings, a recent study found that hypertension was linked with multivessel disease in younger patients with ACS (13). Notwithstanding, in that study, the younger age group consisted of patients under 45 years of age, and only 40% of them had STEMI. In our study, hyperlipidemia was significantly more prevalent in the patients with multivessel CAD. Several studies have reported that the LDL cholesterol values of the majority of young patients with ACS did not require the initiation of medical therapy as per the current guidelines, and this has led to inadequate primary prevention in this patient group (14,15). Hyperlipidemia is a major risk factor for the development of multivessel disease (16).

Previously, marked elevation of non-HDLcholesterol has been found in patients under 40 years of age with ACS compared to age-matched normal individuals (17). However, to the best of our knowledge, there is no study available in the literature that has investigated younger STEMI patients in relation to coronary artery involvement. Another remarkable finding of our study with regard to the patients' lipid parameters was the low HDL-C values. While the LDL cholesterol (LDL-C) values were higher in the patients with multivessel CAD compared to those with single-vessel CAD, the HDL-C values were lower in the former. However, the between-group differences were statistically non-significant. With a larger sample size, it may be possible to detect significant differences between the HDL-C and LDL-C values of the study groups. Smoking and family history have been identified as important risk factors for younger patients with ACS (18,19). Both of these risk factors are more prevalent in younger patients with ACS than their older counterparts. Although the prevalence of smoking in our sample was similar to that reported in previous patient series, family history was less common. In our study, comparable rates of these two risk factors were found among the patients with multivessel CAD and those with single-vessel CAD.

An assessment of the blood parameters of our patients revealed significantly lower hemoglobin values in the patients with multivessel CAD compared to the patients with single-vessel CAD (Figure 2). Anaemia was more common in the patients with multivesselCAD.Anaemia is a significant risk factor for cardiovascular diseases (20). Anemia was associated with mortality and bleeding in one study involving STEMI patients (21). In another study of patients undergoing PCI for ACS, anemia was found to have an impact on both short- and long-term mortality. The effect of anemia on long term mortality was significant

in incomplete revascularization group and multivessel disease group (22). Anaemeia was defined as one of the predictor of hospital readmission in STEMI patients with multivessel PCI inindex hospitalisation (23). It's also showed that anaemia is a predictor of outcome in STEMI patients treated with primary PCI especially in men. It's speculated that Hb levels are effective on mortality only at lower values under 13g/dl (24). It has been suggested that anemia on admission in the setting of an acute MI is at least partly secondary to the initial proinflammatory response (25). Accordingly, a large ischemic area and a more intense inflammatory response may be present in patients with previous involvement of multiple coronary arteries. The higher prevalence of anaemia observed in the acute STEMI patients with multivessel involvement up to 40 years of age in our series may be associated with increased inflammation. The red cell distribution width (RDW) may be elevated in response to increased inflammation in CAD, as well as iron-deficiency anemia (26). Higher mean RDW values were consistently found in the patients with multivessel disease compared to those with single-vessel disease, but the elevation was statistically non-significant.

Our study had a few limitations. These include the retrospective design of the study,the lack of investigation into the specific etiology in the younger patients (e.g.substance use, Kounis syndrome) and the use of the same age range for females and males.

CONCLUSION

In conclusion, we determined that multivessel disease was more commonly associated with male sex, hyperlipidemia and anemia in a sample of STEMI patients under 40 years of age.A better understanding of the clinical characteristics of younger patients with ACS could improve primary and secondary prevention in these patients.

Competing interests: The authors declare that they have no competing interest.
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