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The Prevalence, Clinical Spectrum and the Long Term Outcome of ST-segment Elevation Myocardial Infarction in Young — A Prospective Observational Study☆,☆☆

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ABSTRACT

Introduction: Incidence of coronary artery disease at the younger age is rising. We studied the prevalence, clinical spectrum and long term outcome of ST-segment elevation myocardial infarction in young.
Material and methods: This is a prospective observational study, performed at a tertiary care center from January 2015 to June 2016. Of the total 977 consecutive patients with ST segment elevation myocardial infarction (STEMI), 130 patients aged ≤45 years were included. All patients were followed-up for at least 1-year from the index admission.
Results: The overall prevalence of STEMI among younger patients was 12.8%. There was male dominance (96.8%). Smoking (37.6%) was observed to be the most common risk factor for young STEMI, followed by diabetes mellitus (16.8%) and hypertension (16%). Younger patients with acute MI had preponderance to anterior wall (68.8%), single-vessel disease (50%) and left anterior descending artery being the culprit lesion (67.3%). Near normal/normal coronary arteries were observed in 12.9% of cases. The most commonly used management strategy was mechanical revascularisation (43.2%), followed by thrombolysis (28.8%) and medical management (28%). The overall mortality and combined MACCE rates at 1 year were 3.2% and 18.4% respectively. Outcome was better in patients who received mechanical revascularization/thrombolysis than those who received medical management only, with a lower MACCE rates (hazard ratio: 0.36; 95% CI: 0.16–0.8, p = 0.01.
Conclusion: The young MI patients are unique in having male dominance, better outcome, more of single-vessel disease with significant number of normal coronaries, better response to mechanical as well as pharmacological revascularization.

1. Introduction

Coronary artery disease (CAD) represents the leading cause of mortality in adults. The incidence of myocardial infarction (MI) increases after the age of 45 years. Fortunately, the incidence of MI is low at ages below 45 years [1]. However, the disease at younger age carries a high burden in terms of psycho-social effects, morbidity, and economical loss for patients and their families. The increasing incidence of CAD in the younger age group can be attributed to factors such as smoking, sedentary life styles and childhood obesity [2].

Approximately 10% of patients diagnosed with CAD are <45 years of age [3]. The Asian ethnic population exhibit early age of onset of CAD. However, contemporary data about the clinical characteristics, presentations, angiographic extent of CAD and mortality rates of young patients with AMI are limited. We conducted a prospective study to examine the clinical characteristics, prevalence, and outcomes of patients of acute MI who present at ≤45 years of age.

2. Material and methods

2.1. Study population

This is a prospective study that was performed at a tertiary care center from January 2015 to June 2016. A total of 977 consecutive patients were admitted to our hospital with ST segment elevation myocardial infarction (STEMI). Of these patients, one hundred thirty were aged ≤45 years, presented to our center within 4 weeks of diagnosis and were included in the study. The diagnosis of MI was based on the

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clinical, electrocardiographic and enzymatic data. The follow-up was completed by 96% of the study group, and five patients were lost for various reasons.

Exclusion criteria

- Age > 45 years
- The patient presented >4 weeks after STEMI
- The patients had undergone a prior coronary revascularization procedure

All patients were examined thoroughly, and the relevant investigations were performed. Body mass index (BMI) was calculated form height and weight of patients. Patients with BMIs > 30 were referred to as obese, and those with BMIs between 25 and 30 were referred to as overweight. All patients were managed as per the guidelines. The study protocol was approved by our institutional ethics committee. Informed consent was acquired from all enrolled patients. The 1-year follow up from the index event was completed by 96% of the study population. The clinical events, including all cause death, recurrent MI, cerebro-vascular events, or target vessel revascularisation (TVR) were studied at regular interval of 3 months, 6 months, and 1-year. Data collection was performed either by interviewing the patient in the out-patient department or in the hospital if the patient was admitted, or by telephone communication.

2.2. Definition

Diabetes was defined by either a fasting glucose level was ≥126 mg/dL (7.0 mmol/L) or the patient's current use of an oral hypoglycaemic agent. Dyslipidaemia was labelled by a fasting total cholesterols level was ≥200 mg/dL or the use of hypolipidaemic drugs. Current smoker was defined by active smoker or smoking within the previous 6 months. Hypertension was labelled by either a blood pressure ≥ 140/90 mm Hg or receiving antihypertensive treatment. A family history of premature coronary artery disease was defined by its occurrence before the age of 55 years in a first degree male relative or before the age of 65 years in a first degree female relative. Normal-near normal coronary arteries were defined as those that either had epicardial vessels with no focal lesions and with normal contouring (normal) or minimal luminal narrowing of <30% of the diameter stenosis (near normal).

2.3. Management protocol

All STEMI patients were management according to the guidelines [4]. All patients received loading doses of aspirin and clopidogrel. Revascularisation strategy used was either thrombolysis or percutaneous coronary intervention (PCI) after informed consent. The thrombolytic agent used was either streptokinase or tenecteplase. PCI was offered to the patients as primary, rescue or elective according to the mode of presentation and the delay in presentation of STEMI. Coronary artery bypass grafting (CABG) was offered as the clinical scenario and the coronary anatomy dictated. The patients who did not opt for any mode of revascularization were maintained on conservative management. Dual antiplatelet therapy was maintained for at least one year from the index admission for all forms of therapy.

2.4. Statistical analysis

Continuous and categorical variables are presented as the mean ± the SDs or the medians and frequencies or percentages. For the comparison of the continuous and categorical variables, the Student's *t*-test and chi-square test were used, respectively for normally distributed data, and the Mann-Whitney test and Fischer exact test were used, respectively, for non-normally distributed data. The significance of the MACCE events at the long term follow up was studied using Cox proportional-hazards regression analysis.

3. Results

From January 2015 till June 2016, 125 (12.8%) of a total 977 STEMI patients were included in the study according to the inclusion criteria. All patients were followed up for at least one year from the index admission.

3.1. Patient characteristics

The average age of the study group was 39 ± 6.3 years with a minimum age of 21 years. The distribution of patients according to the delay in presentation after STEMI has been shown in the pie-chart (Fig. 1). Males accounted for 96.8% of the cases. The average follow-up time for the study group was 300 ± 75 days. Smoking (37.6%) was found to be the major risk factor for young STEMI patients and followed by the diabetes mellitus, systemic hypertension, and obesity with almost equal frequencies. The risk factor profile of the study population is tabulated in Table 1.

The most common STEMI location was the anterior wall (68.8%). The most common presenting symptom was angina (80.8%) followed by dyspnea and sweating/diaphoresis in decreasing order. At the time of presentation, 5.6% of the patients were in Killip class III/IV. The average left ventricular ejection fraction (LVEF; %) of the group was 36.9 ± 6.4, and approximately three-fourths of the patients had LVEF between 31 and 40%.

3.2. Management strategy and angiographic profile

Among the study group, 43.2% of the patients had undergone percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) and approximately one quarter of the patients received thrombolytic therapy and optimal medical management each. Of all patients, only 62 patients underwent coronary angiogram. Single-vessel disease was observed in the majority of the patients (50%), and double- and triple-vessel disease was noted in 25.8% and 11.3% of the patients, respectively. Interestingly, normal or near normal coronary arteries

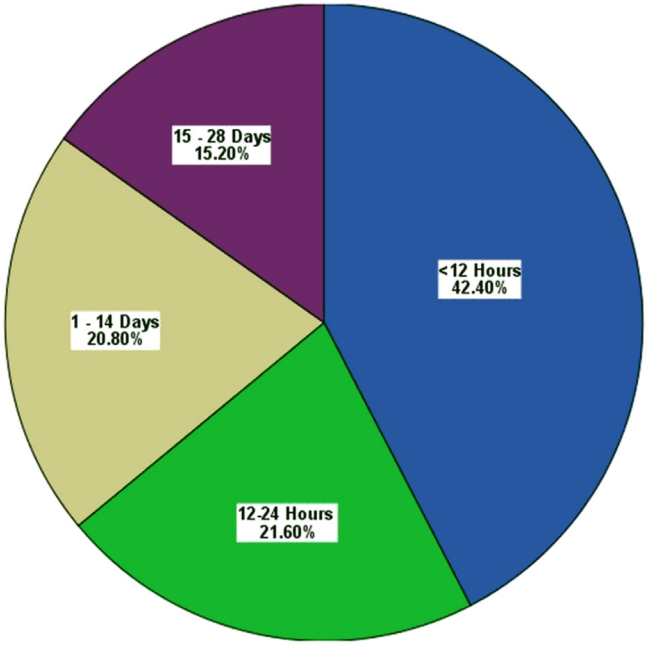

Fig. 1. The pie-chart showing the distribution of patients according to delay of presentation after myocardial infarction.

Table 1
The demographic profile of the study patients. CAD: coronary artery disease.

Age (in years) mean ± SD	39 ± 6.3
Male gender n (%)	121 (96.8%)
Smoking n (%)	47 (37.6%)
Diabetes n (%)	21 (16.8%)
Hypertension n (%)	20 (16%)
Obesity n (%)	21 (16.8%)
Family history of premature CAD n (%)	8 (6.4%)
Dyslipidaemia n (%)	18 (14.4%)
Mean follow up (in days)	300 ± 75

(N/NNCAs) were observed in 12.9% of the cases. The left anterior descending artery was found to be the culprit artery in the majority of the cases followed by the right coronary and left circumflex artery in almost equal proportions.

The clinical profiles, angiographic data and treatment strategies are tabulated in Table 2.

3.3. Clinical outcome

In our study, the in-hospital mortality was 1.6% (n = 2), and the overall morality at 1-year of follow up was 3.2% (n = 4). The incidence of combined MACCE was 18.4% (n = 23). The clinical outcomes were compared between those who received any mode of revascularization i.e., mechanical revascularization (PCI or CABG) or thrombolysis (group 1) and those who received medical management (group 2). The group characteristics are presented in Table 3. All parameters were matched with the exception of smoking; there were significantly more smokers in group 2. The rate of MACCE in Group 1 was significantly lower than in group 2 (p = 0.008). Cox proportional hazards regression analysis revealed that the incidence of MACCE was significantly lower in group 1 than in group 2 with a hazard ratio of 0.36 (95% CI, 0.16–0.8), p = 0.01 (Fig. 2). A sub-group analysis of group 1 revealed that the cumulative hazard far MACCE was non-significantly lower among the patients who underwent mechanical revascularization (PCI/CABG) than among those who received thrombolysis alone (Fig. 3).

Table 2
Table demonstrating the clinical characteristics, angiographic profile, and the treatment strategy. MI: myocardial infarction, LVEF: left ventricular ejection fraction, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting, LAD: left anterior descending, RCA: right coronary artery, LCX: left circumflex, MACCE: major adverse cardiovascular and cerebrovascular events.

Location of MI n (%)	
Anterior wall MI	86 (68.8%)
Inferior wall MI	39 (31.2%)
Presenting symptoms n (%)	
Angina	101 (80.8%)
Dyspnea	14 (11.2%)
Diaphoresis	6 (4.8%)
Killip class IV n (%)	7 (5.6%)
LVEF at admission (mean ± SD)	36.9 ± 6.4
LVEF n (%)	
≤30%	14 (11.2%)
31–40%	73 (58.4%)
>40%	38 (30.4%)
Management strategy n (%)	
PCI/CABG	54 (43.2%)
Thrombolytic therapy	36 (28.8%)
Medical management	35 (28%)
Thrombolytic agent n (%)	
Tenecteplase	19 (51.4%)
Streptokinase	18 (48.6%)
Number of vessel disease n (%)	
Single vessel disease	31(50%)
Double vessel disease	16 (25.8%)
Triple vessel disease/left main disease	7 (11.3%)
Normal/near normal coronary artery(N/NNCAs)	8 (12.9%)
PCI strategy n (%)	
Primary/rescue PCI	20 (38.5%)
Elective PCI	32 (61.5%)
Culprit vessel n (%)	
LAD	35 (67.3%)
RCA	8 (15.4%)
LCX	9 (17.3%)
In-hospital mortality n (%)	2 (1.6%)
Mortality at 1-year n (%)	4 (3.2%)
MACCE at 1-year n (%)	23 (18.4%)

Table 3
Demographic and clinical parameters of both the groups. PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting, CAD: coronary artery disease, MI: myocardial infarction, LVEF: left ventricular ejection fraction, MACCE: major adverse cardiovascular and cerebrovascular events.

		PCI/CABG/thrombolysis (group 1) n = 90	Medical management (group 2) n = 35	p value
Age (years)		39.4 ± 5.7	38.3 ± 6.9	0.521
Male n (%)		86 (95.6%)	35 (100%)	0.582
Smoking n (%)		28 (31.1%)	19 (54.3%)	0.022
Diabetes mellitus n (%)		15 (16.7%)	6 (17.1%)	0.953
Hypertension n (%)		14 (15.6%)	6 (17.1%)	0.833
Obesity n (%)		16 (17.8%)	5 (14.3)	0.792
Dyslipidaemia n (%)		13 (14.4%)	5 (14.3%)	0.994
Premature CAD n (%)		6 (6.7%)	2 (5.7%)	0.994
Location of MI	Anterior wall MI	60 (66.7%)	26 (74.3%)	0.412
	Inferior wall MI	30 (33.3%)	9 (25.7%)	
LVEF at admission (%)		37.3 ± 6.3	35.6 ± 6.5	0.156
MACCE at 1 year follow-up		12 (13.3%)	12 (34.3%)	0.008

3.4. Smoker subset

All patients were male with the average age of 38.4 ± 6.2 years. Compared to non-smokers, various factors like location of MI, clinical presentation, LVEF at admission were comparable in smokers. Table 4 describes the clinical profile of smoker subset. Compared to non-smokers, majority of the smoker patients had received either thrombolytic therapy or optimal medical management while less number of patients received mechanical revascularisation (PCI/CABG) (p = 0.001). Despite of that, the clinical outcome in term of overall mortality

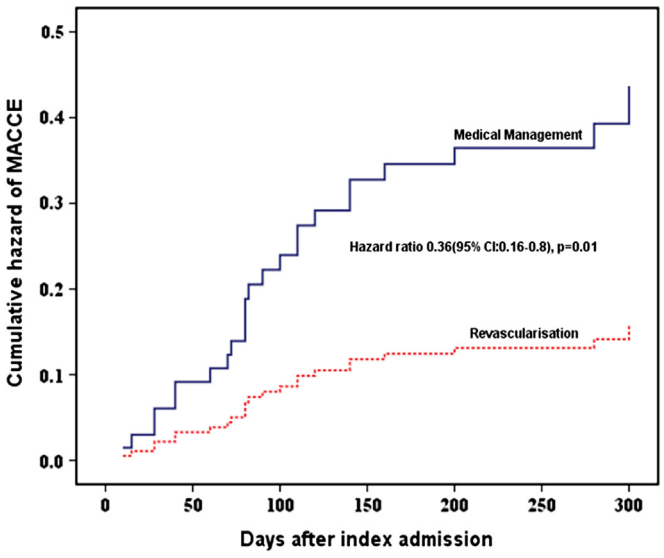

Fig. 2. Cox proportional hazards regression analysis for MACCE rate at 1-year for patients receiving revascularization (PCI/CABG/thrombolysis) therapy versus medical management. MACCE: major adverse cardiovascular and cerebrovascular event, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting.

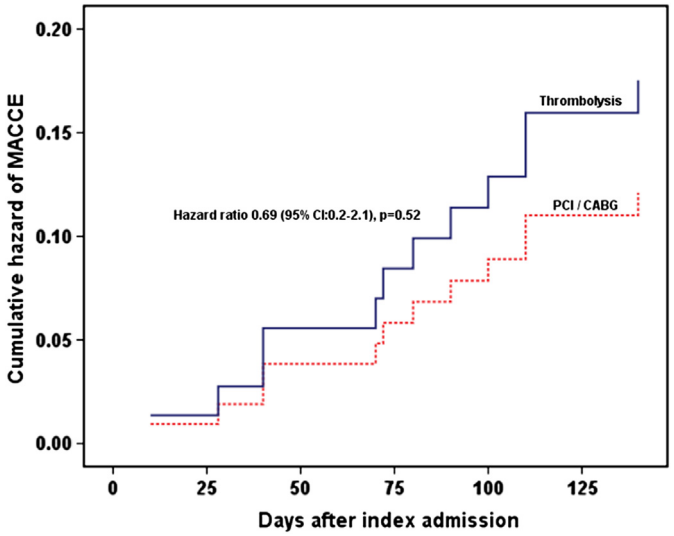

Fig. 3. Cox proportional hazards regression analysis for MACCE rate at 1-year for patients receiving mechanical revascularization (PCI/CABG) versus thrombolytic therapy. MACCE: major adverse cardiovascular and cerebrovascular event, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting.

and MACCE at 1-year was comparable between smokers and non-smokers ($p = 0.9$).

4. Discussion

Coronary artery disease (CAD) is becoming more prevalent due to the increasing trends of diabetes, smoking, sedentary life-styles etc. CAD in the young is an altogether different entity due to its different risk profile, social acceptance and clinical outcomes. In this study, we attempted to identify the demographic characteristics and outcomes in STEMI subset of young CAD patients.

The prevalence of young STEMI was 12.8% in our study, while the literature quotes 2–11% of the admitted myocardial infarctions are premature [3,5]. The higher prevalence observed in our study probably reflects the rising trends of childhood obesity, smoking at an early age, stress, and sedentary life-style [6]. Similar to our study, the young STEMI patients are dominated by the males in the literature as well. Due to its increasing prevalence among the young, the smoking is considered to be the most common risk factor for the development of CAD. Various studies have demonstrated that family history of premature CAD and smoking are the common risk factors for the young CAD [7,8]. Among all of the studied risk factors, our study found smoking to be the factor that most commonly influenced the occurrence of CAD in the young.

Similar to our study, a few studies have reported the anterior wall to be the most common site of STEMI [9,10], while other studies suggest that the inferior wall is the most common site [11,12]. The clinical presentation STEMI in the young usually involves new onset, rapidly progressive angina with no prior history of stable angina, whereas the elderly age group exhibits a higher incidence of prior warning symptoms [13]. A prior history of stable angina has been noted in only approximately 24% of cases [13]. Similarly, our study also exhibited acute onset angina as the most common presentation. We observed a relatively higher incidence of Killip class III/IV, patients compared to previous studies that have reported an incidence of approximately 3%. Some studies have reported higher incidences (6.7%) of Killip class III/IV patients [14].

Consistent with previous studies, single-vessel disease (most commonly in the left anterior descending artery) was present in the majority of patients, and the percentage of patients with normal/near normal coronary arteries was quite high (12.9%) [5,15,16]. Various studies have reported incidences of normal coronary arteries in young myocardial infarction (MI) patients of approximately 9% to 17% [17,18]. Notably, based on various studies the younger patients with MI have lower atheromatous plaque burden but more thrombotic lesions.

Compared to the previously reported data [19], reperfusion therapy, either mechanical (PCI/CABG) or pharmacological (thrombolysis), was used more frequently in our study. A study by Morillas et al. reported the use of reperfusion therapy in 62.2% (fibrinolytic therapy in 55.55% and PCI in 6.7%) of cases of young MI [14]. Due to increasing ease access to, and the wider availability of catheterisation laboratories, the use PCI for the management of acute MI has increased, which could account for the fact the greatest number of patients received PCI thereby our study have more number of patients in our study received initial PCI which was followed by thrombolysis and medical management at almost equal frequencies. A study by Cole et al. demonstrated that the outcomes of younger patients who undergo PCI or CABG are better due to reduced post-procedural complications and the good success rates [7,20]. Various studies have demonstrated the favourable outcome of the thrombolytic therapy in young MI patients compared to older patients. This difference has been postulated to be due to greater thrombotic burden than atherogenic burden and reduced association with co-morbidities, such as hypertension and diabetes, among younger patients who produce better response to fibrinolytic therapy [3,5,7,8,11,20,21]. Similarly in our study, the event-free survival was significantly better among those who received revascularization therapy (PCI/CABG/thrombolysis) than those who received medical management alone. Among the revascularization group, the mechanical mode of revascularisation (i.e., PCI and CABG) resulted in non-significantly better event-free survival than thrombolysis. Thus, thrombolysis is not inferior to mechanical mode of revascularisation for young MI patients. Age is considered to be the major determinant of both short- and long-term mortality, younger patients exhibit longer survival time [3,11,22]. Our study found an in-hospital mortality rate of 1.6%, while various other studies have reported mortality rates ranging between 2.5 and 3.4% [14,23]. Another study demonstrated lower mortality among young MI patients with 28 day and 1-year mortality rates of 3.7% and 4.3%, respectively [24]. Similar to these studies, suggestive of the favourable outcomes for young MI patients, our study found low in-hospital and long term mortality rates. Among the smokers, the clinical outcome was comparable to those of non-smokers irrespective of the mode of revascularisation therapy. The probable reason could be due to the high success rate with thrombolytic therapy among smokers who are supposed to have thrombotic occlusions.

Table 4
Demographic profile of the study group in smoker subgroup.

Age (in years) mean ± SD	38.4 ± 6.2
Male Gender n (%)	47 (100%)
Diabetes n (%)	7 (14.9%)
Hypertension n (%)	3 (6.4%)
Obesity n (%)	3 (6.4%)
Family history of premature CAD n (%)	3 (6.4%)
Dyslipidaemia n (%)	3 (6.4%)
Mean follow up (in days)	294 ± 66

5. Conclusion

The overall prevalence of STEMI among young patients observed in this study was high compared to the results of prior studies. Therefore there is a need to focus at the level of primordial and primary prevention. There was a male preponderance in the present group of patients. Smoking remains the most common predisposing factor for younger patients. With the available revascularization therapies, the long-term outcome is good. In present-day scenario, there is a trend toward the increased use of PCI as the preferred mode of revascularization. Thrombolytic therapy still has a role in the treatment of young MI

patients due to the high incidence of thrombotic lesions and especially so among smoker patients.

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