

Acute myocardial infarction: Clinical features and outcomes in young adults in Singapore

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Abstract

AIM: To investigate the clinical features and in-hospital outcomes of young adults with acute myocardial infarction (AMI) in Singapore.

METHODS: Between January 2005 to September 2010, 333 consecutive patients aged ≤ 45 years old were diagnosed to have AMI at our institution. As Singapore is a multi-ethnic society, we also analysed whether ethnic differences exist between the three dominant ethnic groups, Malay, Chinese and Indian with regards to the clinical features. Clinical data was collected retrospectively on demographic characteristics, presenting signs and symptoms, blood investigation, angiographic findings and in-hospital clinical outcomes.

RESULTS: The mean age at presentation was 40.2 ± 4.0 years with male predominance (94%). The majority of patients were Chinese (51%) followed by Indians (31%) and Malays (18%). The most common risk factor was smoking (74%) followed by hypertension (28.5%) and hyperlipidemia (20.0%). 37% of patients were obese. The majority of patients had single vessel disease (46%) on coronary angiography. The mean

total cholesterol, low-density lipoprotein and high-density lipoprotein levels were 5.6 ± 1.2 mmol/L, 3.8 ± 1.1 mmol/L and 0.93 ± 0.25 mmol/L respectively. The mean left ventricular function was $44\% \pm 10\%$ with the incidence of heart failure 3% and cardiogenic shock 4.5%. Overall in-hospital mortality was low with 4 deaths (1.2%). For ethnic subgroup analysis, Indians have a 3-fold risk of developing premature AMI when compared to other ethnic groups.

CONCLUSION: Young AMI patients in Singapore are characterized by male predominance, high incidence of smoking and obesity. Overall in-hospital clinical outcomes are favourable. Among the 3 ethnic groups, Indians have the highest risk of developing premature AMI.

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Key words: Clinical features; Myocardial infarction; Outcomes; Southeast asia; Young

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INTRODUCTION

Acute myocardial infarction (AMI) is a major cause of morbidity and mortality worldwide. The burden of AMI can be substantial if the individual is relatively young as they are commonly breadwinners of the family and in the prime of their working life with significant contributions

to the society. Several studies^[1-12] have described the clinical profiles and outcomes of young adults with AMI and its incidence ranged between 2% and 10%. In general, young patients are more likely to be male, have a history of smoking and hyperlipidemia but less likely to have other comorbidities and demonstrate less extensive coronary artery disease (CAD) on coronary angiogram. There is limited data^[11,12] on the clinical features of young adults with AMI in the Southeast Asian region. We therefore sought to investigate the clinical characteristics, angiographic findings and clinical outcomes (in-hospital) of young adults with AMI in Singapore. As Singapore is a multi-ethnic society, we also analysed whether ethnic differences exist between the three dominant ethnic groups i.e., Malay, Chinese and Indian with regards to the clinical features.

MATERIALS AND METHODS

Study population

Between January 2005 to September 2010, 333 consecutive patients aged ≤ 45 years old were diagnosed to have AMI at our institution, a tertiary referral centre in Singapore. Clinical data was collected retrospectively from the medical records on demographic characteristics, presenting signs and symptoms, blood investigation, angiographic findings and in-hospital clinical outcomes.

The diagnosis of AMI was defined as the presence of chest pain and/or electrocardiographic changes suggestive of infarction or ischaemia, associated with increased level of cardiac troponins or cardiac enzymes to at least twice the upper limit of the normal value. All the study patients underwent coronary angiography during the index hospitalisation. Angiographic stenosis was defined as diameter reduction of $\geq 50\%$. The culprit artery for AMI was identified based on morphology including complete occlusion, thrombus and ulcerative stenosis or assumed to be the tightest stenosis if these features were absent. The classification of body weight by body mass index (BMI) was according to the World Health Organization recommendation for an Asian population^[13]. A BMI of more than 27 kg/m^2 was defined as obese. The major clinical outcomes (in-hospital) analysed in our study include all-cause mortality, congestive heart failure (New York Heart Association class III-IV), major arrhythmia events (complete heart block, ventricular tachycardia/fibrillation) and cardiogenic shock.

Subgroup analysis by ethnicity

Singapore is a Southeast Asian city-state which has a multi-ethnic population of 5.1 million. There are 3 dominant ethnic groups namely, Malays, Chinese and Indians with the rest being a mixture of minority ethnic group/foreigners. Based on the government census report, the racial composition of Malays, Chinese and Indians in the general population were 13.4%, 74.2% and 9.2%, respectively.

Statistical analysis

Continuous variables were expressed as mean \pm SE of mean. Dichotomous variables were expressed as counts

and percentages. Statistical comparisons were performed using analysis of variance (ANOVA) and chi square test for trend, as appropriate. A statistically significant effect in ANOVA is followed up by Tukey's range test. Calculations were performed using SPSS software (version 16.0; SPSS, Inc., Chicago, Illinois). All *P* values were 2-sided and *P* values < 0.05 were considered statistically significant. All investigations were carried out in accordance with the Declaration of Helsinki and the study was approved by the local ethics committee.

RESULTS

Table 1 shows the baseline clinical characteristics of our patients. For the overall study group, the mean age at presentation was 40.2 ± 4.0 years (range 25 to 45 years) with male predominance (94%). The most common risk factor was smoking (74%) followed by antecedent hypertension (28.5%), hyperlipidemia (20%) and diabetes mellitus (16.5%). The mean BMI was $26.1 \pm 3.8 \text{ kg/m}^2$ with 37% of young adults considered obese by Asian BMI criteria. The most common risk factor newly identified at presentation was hyperlipidemia (28%) followed by diabetes mellitus (13%) and hypertension (3%). The mean total cholesterol, low-density lipoprotein and high-density lipoprotein levels were $5.6 \pm 1.2 \text{ mmol/L}$, $3.8 \pm 1.1 \text{ mmol/L}$ and $0.93 \pm 0.25 \text{ mmol/L}$ respectively. For those with pre-existing diabetes mellitus, the mean HbA1c level was $7.7 \pm 2.3 \text{ mmol/L}$. The mean left ventricular function was $44\% \pm 10\%$. The mean peak creatine kinase was $2227 \pm 2389 \text{ IU/L}$ and Troponin-I level was $36.0 \pm 33.7 \mu\text{g/L}$.

Table 2 shows the clinical presentation, angiographic findings, procedural variables and clinical outcomes of our patients. The majority of patients presented with ST-elevation MI (66.3%) with a slightly higher rate of inferior-posterior MI than anterior MI. By angiographic analysis, the majority of patients (46%) had single vessel disease followed by double vessel disease (26%) and triple vessel disease (23.4%). Occlusive left main disease was present in 11 patients (3.3%) and 14 patients (4.2%) had normal coronary vessels. Two hundred and forty two patients (73%) were treated with percutaneous coronary intervention (PCI) with the rest receiving medical therapy (thrombolysis/anti-thrombotic therapy). The mean number of stents per patient was 1.32 ± 0.65 , mean stent diameter was $3.05 \pm 0.64 \text{ mm}$ and the average length of stents was $21.7 \pm 6.9 \text{ mm}$. The majority of patients (67%) had bare metal stent implantation during PCI.

Overall in-hospital mortality was low with 4 deaths (1.2%). Three patients died due to complications of AMI whereas the 4th patient died of in-hospital sepsis. The incidence of heart failure was 3% and cardiogenic shock was 4.5%. Only 10 patients (3%) required intraaortic balloon counterpulsation for hemodynamic support. The incidence of major arrhythmia events was 7.2%.

Subgroup analysis by ethnicity

Figure 1 shows the relative risk of each ethnic group for developing AMI in relation to racial composition in the

Table 1 Baseline clinical characteristics of patients

	Overall (n = 333)	Malay (n = 59)	Chinese (n = 171)	Indian (n = 103)	P value
Mean age at presentation (yr)	40.2 ± 4.0 (25-45)	40.3 ± 4.8 (25-45)	40.4 ± 3.6 (30-45)	39.9 ± 4.2 (26-45)	0.62
Male:female	329:23 (93.5:6.5)	53:6 (89.8:10.2)	160:11 (93.6:6.4)	100:3 (97.1:2.9)	0.06
Ever smoker	246 (73.8)	48 (81.4)	127 (74.3)	71 (68.9)	0.08
Hypertension	95 (28.5)	15 (25.4)	54 (31.6)	26 (25.2)	0.78
Hyperlipidemia	66 (19.8)	10 (16.9)	32 (18.7)	24 (23.3)	0.28
Diabetes	55 (16.5)	10 (16.9)	23 (13.5)	22 (21.4)	0.31
Mean BMI (kg/m ²)	26.1 ± 3.8	26.2 ± 4.7	25.8 ± 3.6	26.7 ± 3.7	0.15
Newly diagnosed hyperlipidemia	93 (27.9)	19 (32.3)	49 (28.7)	25 (24.3)	0.26
Newly diagnosed diabetes	43 (12.9)	3 (5.1)	23 (13.5)	17 (16.5)	0.04 ^a
Newly diagnosed hypertension	9 (2.7)	5 (8.5)	2 (1.2)	2 (1.9)	0.04 ^a
Mean total cholesterol (mmol/L)	5.6 ± 1.2	5.9 ± 1.1	5.6 ± 1.2	5.5 ± 1.3	0.16
Mean LDL (mmol/L)	3.8 ± 1.1	4.1 ± 1.1	3.7 ± 1.0	3.8 ± 1.1	0.08
Mean HDL (mmol/L)	0.93 ± 0.25	0.92 ± 0.22	0.95 ± 0.27	0.89 ± 0.22	0.14
Mean HbA1c (mmol/L)	7.7 ± 2.3	7.7 ± 2.3	7.4 ± 2.3	8.15 ± 2.4	0.04 ^a
LVEF (%)	44 ± 10	41 ± 10	45 ± 9	43 ± 11	0.008 ^a
Creatine kinase (IU/L)	2227 ± 2389	1870 ± 2064	2350 ± 2656	2220 ± 2055	0.41
Troponin (ng/mL)	36 ± 34	32 ± 34	36 ± 34	38 ± 33	0.55

^aP < 0.05. BMI: Body mass index; LDL: Low density lipoprotein; HDL: High density lipoprotein; HbA1c: Glycosylated hemoglobin; LVEF: Left ventricular ejection fraction.

Table 2 Clinical presentation, angiographic findings, procedural variables and clinical outcomes (in-hospital) of patients

	Overall (n = 333)	Malay (n = 59)	Chinese (n = 171)	Indian (n = 103)	P value
Presentation					
Anterior STEMI	109 (32.7)	19 (32.2)	59 (34.5)	31 (30.1)	0.68
Inferior/posterior STEMI	112 (33.6)	14 (23.7)	59 (34.5)	39 (37.9)	0.08
NSTEMI	112 (33.6)	26 (44.1)	53 (31.0)	33 (32.0)	0.18
Number of diseased vessels on angiography					
0	14 (4.2)	1 (1.7)	10 (5.8)	3 (2.9)	0.95
1	153 (45.9)	23 (39)	78 (45.6)	52 (50.5)	0.15
2	88 (26)	18 (30.5)	45 (26.3)	25 (24.3)	0.40
3	78 (23.4)	17 (28.8)	38 (22.2)	23 (22.3)	0.40
Left main	11 (3.3)	2 (3.4)	8 (4.7)	1 (1.0)	0.27
Procedural variables					
DES:BMS	80:162 (33:67)	11:26 (29.7:70.3)	45:79 (36.3:63.7)	24:57 (29.6:70.4)	0.75
Mean number of stents	1.32 ± 0.65	1.41 ± 0.72	1.37 ± 0.69	1.21 ± 0.52	0.14
Mean stent diameter,mm	3.05 ± 0.64	3.03 ± 0.72	3.13 ± 0.57	2.94 ± 0.69	0.11
Stent length,mm	21.7 ± 6.9	21.4 ± 7.3	22.4 ± 7.1	20.8 ± 6.4	0.25
Clinical outcomes					
All-cause mortality	4 (1.2)	0 (0)	2 (1.2)	2 (1.9)	0.27
Congestive heart failure	10 (3.0)	2 (3.4)	3 (1.8)	5 (4.9)	0.43
Major arrhythmic event	24 (7.2)	1 (1.7)	17 (9.9)	6 (5.8)	0.32
Cardiogenic shock	15 (4.5)	0 (0)	9 (5.3)	6 (5.8)	0.12

STEMI: ST-elevation myocardial infarction; NSTEMI: Non ST-elevation myocardial infarction; DES: Drug eluting stent; BMS: Bare metal stent.

general population. Indians have a 3-fold risk of developing AMI before age of 46 compared to Malays (1.25-fold risk) and Chinese (0.7-fold risk) respectively. As shown in Table 1, there was no significant difference between the 3 ethnic groups with regards to antecedent cardiovascular risk factors. Indians were however more likely to be diagnosed with new-onset diabetes mellitus at presentation and also, have the highest HbA1c values in pre-existing diabetics when compared with the other ethnic groups. On the other hand, Malays were more likely to be diagnosed with new-onset hypertension at presentation when compared to the rest. As shown in Table 2, there was no significant difference among the 3 ethnic groups in terms of clinical presentation and severity of CAD by coronary

angiography. The incidence of in-hospital major complications and in-hospital mortality also did not differ between the 3 ethnic groups. Although there were ethnic differences in the mean left ventricular function (Table 1), this did not translate to any significant difference in the clinical outcomes.

DISCUSSION

To our knowledge, this is the largest cross-sectional study looking at the clinical profile of young adults with AMI in the Southeast Asian region. Young adults represented 8%-12% of all AMIs during the 5-year study period. Our study demonstrated that young adults with AMI in

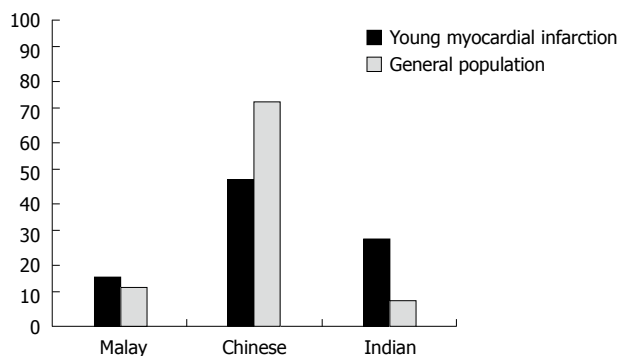


Figure 1 Relative risk of premature acute myocardial infarction of different ethnic groups in relation to racial composition in the general population.

Singapore are characterized by male predominance, high incidence of smoking and obesity. This is consistent with findings of prior studies^[1-12] in which young patients are more likely to be male, have a history of smoking and hyperlipidemia but less likely to have other co-morbidities. Smoking remains the single most important modifiable risk factor in causing premature MI in all the reported studies^[1-12,14]. This is also confirmed in our study as 74% of our patients had history of tobacco use. The other common risk factors are antecedent hyperlipidemia and hypertension with varying rates of prevalence reported in different studies. In our study, 28.5% of patients had antecedent hypertension and 20% had antecedent hyperlipidemia. On the other hand, 16.5% of patients had antecedent diabetes mellitus and this rate is relatively high (> 10%) when compared to other studies. Obesity is also a common risk factor in our patients as 37% were found to be obese at presentation. Both these risk factors are likely a reflection of the rising rate of metabolic syndrome^[15,16] in Asia which is increasingly recognised as a growing public health problem.

Previous studies^[1-11] have shown that young patients demonstrated less extensive CAD on coronary angiogram ie the majority of patients had single vessel disease. This was also true for our cohort of patients, however, the percentage of single vessel disease was < 50% in our study. On the other hand, the percentages of two vessel disease and triple vessel disease were relatively higher, 26% and 23.4% respectively. These angiographic features suggest that our overall cohort of patients have relatively “extensive” CAD at presentation when compared to patients described in prior studies. This finding have potential implications as it suggests our patients might be at higher risk for future major adverse cardiac events if risks factors are not optimally controlled. They also would have a higher likelihood of needing multi-vessel PCI or coronary artery bypass surgery if the CAD progressed.

As for in-hospital clinical outcomes, only 4 patients (1.2%) died during the index hospitalisation. The incidence of heart failure and cardiogenic shock were 3% and 4.5% respectively. Our findings are consistent with results of prior studies^[1-11] which had shown favourable clinical outcomes for young adults with AMI. This is possibly due to better cardiac reserve for young patients (who

have less co-morbidities) with a better capacity to recover from acute cardiac injury than older patients.

Our study is also one of the few studies^[11,12,17] to examine whether there were ethnic differences in clinical features and outcomes in a multi-ethnic population for premature AMI. A local study (inclusive of residents aged 20 to 64 years old) by Mak *et al*^[18] had shown that the MI event rates rate for Indians and Malays were much higher than Chinese with overall rate ratios of 3.1 and 2.1 respectively. We extended this previous observation in a much younger patient population and demonstrated that Indians have a 3-fold risk of developing premature AMI in comparison to the other ethnic groups. Prior studies^[18-22] have shown that Indians have at least double the risk of CAD than than of white patients after adjustment of risk factors. The causes of this ethnic predisposition to CAD are likely to be multi-factorial ie interaction between genetic and environmental factors. The role of inherited predisposition to coronary thrombosis is limited to certain genetic factors as shown by a recent study^[23] in young north Indian survivors of AMI. More importantly, several studies^[19-22] have shown that Indians are prone to developing metabolic abnormalities at a lower BMI and lower waist circumference. They were also found to have high serum levels of apolipoprotein B (which forms low density lipoprotein) and triglycerides and demonstrated low levels of apolipoprotein A1 and high density lipoprotein. All these factors lead to incremental risk of having metabolic syndrome which acts as a “fertile ground” for the development of diabetes mellitus and premature CAD in Indians.

In our study, Indians were more likely to be diagnosed with new-onset diabetes mellitus whereas Malays were more likely to be diagnosed with new-onset hypertension at presentation when compared to other ethnic groups. The former also had poorly controlled diabetes mellitus in those with pre-existing diabetes mellitus. This suggests subtle differences in the risk factor profile for each ethnic group and can help tailor the focus of primary preventive measures.

There were several limitations to our study. Although our sample size was relatively large, our study was a retrospective non-randomised study from a tertiary referral center, hence, selection bias was inevitable and would impact on our findings. Family history do play an important role in contributing to premature CAD but we were not able to evaluate this association adequately in our study due to lack of query/documentation in medical records.

We found that young adults with AMI in Singapore are characterized by male predominance, high incidence of smoking and obesity. Overall in-hospital clinical outcomes are favourable. Among the 3 ethnic groups, Indians have the highest risk of developing premature AMI. Primary preventive measures with special focus on smoking cessation and early screening for modifiable risk factors of CAD remain the best strategy to prevent AMI in young adults in Singapore. Obesity is a growing problem which needs to be tackled aggressively with early intervention programs. Further studies are needed to assess

the long term clinical outcomes of this group of patients with possible genetic studies to look into each ethnic predisposition for premature CAD.

COMMENTS

Background

Acute myocardial infarction (AMI) is a major cause of morbidity and mortality worldwide. The burden of AMI can be substantial if the individual is relatively young as they are commonly breadwinners of the family and in the prime of their working life with significant contributions to the society. Several studies have described the clinical profiles and outcomes of young adults with AMI but there is limited data on the clinical features of young adults with AMI in the Southeast Asian region.

Research frontiers

The authors therefore sought to investigate the clinical characteristics, angiographic findings and clinical outcomes (in-hospital) of young adults with AMI in Singapore. As Singapore is a multi-ethnic society, the authors also analysed whether ethnic differences exist between the three dominant ethnic groups, Malay, Chinese and Indian with regards to the clinical features.

Applications

The study results showed that young adults with AMI in Singapore are characterized by male predominance, high incidence of smoking and obesity. Overall in-hospital clinical outcomes are favourable. Among the 3 ethnic groups, Indians have the highest risk of developing premature AMI. Primary preventive measures with special focus on smoking cessation and early screening for modifiable risk factors of coronary artery disease remain the best strategy to prevent AMI in young adults in Singapore. Obesity is a growing problem which needs to be tackled aggressively with early intervention programs. Further studies are needed to assess the long term clinical outcomes of this group of patients with possible genetic studies to look into each ethnic predisposition for premature AMI.

Terminology

AMI: Commonly known as a heart attack, results from interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to blockage of a coronary artery which can cause damage or death (infarction) of heart muscle tissue if left untreated for a sufficient period of time; Coronary angiography: A special X-ray evaluation (invasive procedure) of the coronary arteries in which dye is injected down the coronary arteries. The arteries then show up clearly on an X-ray and the exact site and severity of any narrowing of the coronary arteries can be identified; Low density lipoprotein: Commonly known as "bad cholesterol" particles which drive progression of atherosclerosis leading to adverse cardiovascular events and death; High density lipoprotein: Commonly known as "good cholesterol" particles. Higher levels are associated with fewer adverse cardiovascular events and death; Heart failure: The inability of the heart to provide sufficient pump action to distribute blood flow to meet the needs of the body; Cardiogenic shock: Caused by the failure of the heart to pump effectively and is defined by sustained hypotension with tissue hypoperfusion despite adequate left ventricular filling pressure.

Peer review

The authors have performed an interesting descriptive study investigating baseline clinical characteristics and in-hospital outcomes in a total of 333 young AMI patients in Singapore. The authors should be complimented for providing thorough baseline clinical data, angiographic findings and clinical outcomes. The study findings adds important data to the existing literature on premature AMI as data from Southeast Asian region is scarce.

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