Association of Co-Morbidity and Treatment with the Complications of Acute Coronary Syndrome in Young Patients Less Than 45 Years

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Abstract

Background: Approximately 5%–10% of acute coronary syndrome (ACS) cases occur in people younger than 45 years of age. This study aimed to identify complications of ACS and the associated factors in young patients.

Methods: In this cross-sectional study, data from 147 ACS patients aged less than 45 years were analysed.

Results: The mean age was 39.1 (4.9) years, the male to female ratio was 3:1; 21.2% of patients presented with unstable angina, 58.5% had non-ST elevation myocardial infarction and 20.4% had ST elevation myocardial infarction. The most frequent risk factor of ACS was dyslipidaemia (65.3%), followed by hypertension (43.5%). In total, 49.7% of patients had inpatient complication(s), with the most common being heart failure (35.4%), followed by arrhythmia (20.4%). The significant factors associated with ACS complications were current smoking [adjusted odds ratio (AOR) 4.03; 95% confidence interval (CI): 1.33, 12.23; *P*-value = 0.014], diabetic mellitus [AOR 3.03; 95% CI: 1.19, 7.71; *P*-value = 0.020], treatments of fondaparinux [AOR 0.18; 95% CI: 0.08, 0.39; *P*-value < 0.001] and oral nitrates [AOR 0.18; 95% CI: 0.08, 0.42; *P*-value < 0.001].

Conclusions: Smoking status and diabetes mellitus were modifiable risk factors while pharmacological treatment was an important protective factor for ACS complications in young patients.

Keywords: *acute coronary syndrome, unstable angina, non-ST elevation myocardial infarction, ST elevation myocardial infarction*

Introduction

Cardiovascular diseases (CVDs) are the main causes of mortality and morbidity in Malaysia and worldwide. In 2006, the estimated incidence of Malaysian acute coronary syndrome (ACS) was 141 per 100,000 population per year, and the inpatient mortality rate was approximately 7% (1). The Global Registry of Acute Coronary Events (GRACE) reported that 6.3% of patients were aged less than 45 years (2), and in Thailand, 5.8% of ACS patients were under the age of 45 years (3).

ACS has a higher prevalence in middle-aged and elderly patients; thus, comparatively fewer studies have focused on the clinical presentation, treatment and outcome of ACS in young patients. The cut off age of 45 years has been used in most studies to define young patients with ACS (2, 3, 4). The occurrence of ACS in young adults leads to premature morbidity and mortality in the person's most productive years of life. It may adversely affect the physical and psychosocial well-being of the patient, as well as their family. There are differences in the characteristics of young and older patients with ACS. Young patients with ACS commonly present with chest pain but rarely present with heart failure (5). They are more likely to present with ST elevation myocardial infarction (STEMI) (67.3%) than older patients (3).

The most important cardiovascular risk factors in ACS in young patients are smoking, family history of coronary artery disease (CAD), dyslipidaemia and obesity (3, 4, 5). Smoking is an important cardiovascular risk factor that is inversely related to age. The prevalence of smoking ranges from 70%–90% among young ACS patients; smoking was found in up to 92% of young patients with reported atheromatous process (4). Dyslipidaemia and family history of CAD are considered to be important risk factors in young patients. Patients with a family history of CAD tend to have an abnormal lipid profile, especially hypertriglyceridaemia, low high density lipid (HDL), insulin resistance and obesity; this strengthens the theory of a common genetic linkage (3, 4, 6).

Despite this knowledge, the management of ACS in young patients within local settings requires further understanding. Assessing the socio-demographics, clinical presentation, risk factors and complications of ACS in young patients will provide data that are considerably useful in evaluating the effectiveness of management as well as the preventive and control strategies and the intervention strategies for ACS. A high prevalence of risk factors in young ACS patients is likely to indicate that prevention should begin at an early age. In addition, studies on ACS in young patients are limited, and thus, the results of this study may be potentially applicable for further reference and research to the benefit of patients. Therefore, the aim of this study was to identify the characteristics, risk factors, treatment and complications of ACS and the associations in young patients aged less than 45 years.

Materials and Methods

This study was conducted at a teaching hospital in the north-east of Malaysia; this teaching hospital is a government funded medical institution located in Kelantan. The hospital has 747 beds with in-patient services that include medical, paediatrics, newborn-paediatrics, paediatrics surgery, oncology, surgery, neuro-surgery, burn-surgery, psychiatry, charged ward, orthopaedic, ophthalmology, obstetrics, gynaecology, otorhinolaringology, intensive care unit and coronary care unit. Out-patient services include family medicine clinic, specialist clinic services, accident and emergency services and dental clinic. The average attendance to these clinics is 190 000 per year. Around 50% of the admissions are to specialist clinics, 25% to the family medicine clinic, 15% to the accident and emergency unit and 10% to the staff clinic. The average number of in-patient admissions is 28 000 per year. The bed occupancy rate is 56% (7).

This study was a retrospective study that involved reviewing patients' records. The study sample comprised patients aged less than 45 years old, diagnosed with ACS, and admitted to the hospital, who fulfilled the inclusion and exclusion criteria. Patients were eligible for inclusion if they were aged less than 45 years old and were diagnosed with ACS based on symptoms and electrocardiography (ECG) changes that were consistent with ACS, as well as serum biomarkers changes (8, 9, 10). The diagnosis was made by the attending physician and it was the respondent's first admission due to ACS. The exclusion criteria for this study were incomplete medical record of 30% of the variables, and patients who were referred or transferred from other hospitals for further management and who had incomplete admission data from the referral hospital.

The list from the medical record department comprised 196 cases of young patients diagnosed with ACS, aged less than 45 years old for the period between 1 January 2002 and 31 December 2011. No sampling method was applied. All data was extracted using a checklist proforma that consisted of socio-demography, medical history, clinical presentation, investigation and diagnosis, treatment, prognosis and complications. We also collected the earliest results of blood investigations.

Statistical Analyses

All data was analysed using IBM SPSS statistics 22 software. All data were tabulated for descriptive statistics. All categorical variables were summarised as frequencies (n) and percentages (%). The numerical variables were described as means and standard deviations (SD) or medians and interquartile ranges (IQR), depending on the normality of the distribution.

The outcome of this study was a binary variable coded "1" for presence and "0" for the absence of ACS complications. Complications that were considered in this study were those acquired related to ACS, and which occurred after the diagnosis of ACS, as identified and diagnosed by the attending physician during current admission. Complications were considered present when the patients had any of the following: heart failure, pulmonary oedema, arrhythmia, cardiogenic shock, cardiac arrest, recurrent ischaemia, reinfarction or mortality (3, 8, 11).

Multiple logistic regression was used to identify factors associated with complications. The final model is presented with adjusted odds ratios (AOR) and 95% confidence intervals (CI), as well as Wald statistic and P-value. The level of significance was set at P less than 0.05.

The confidentiality of patients in this study was maintained, no name are mentioned and personal information was not identified. The researcher who reviewed the patients' record was not involved in the management of patients. Ethical approval was obtained from the Human Research Ethics Committee, reference USMKK/PPP/JEPeM (256.4 (1.2)). Approval from the Director of Hospital was also obtained prior to the study.

Results

There were 196 patients aged less than 45 years who were diagnosed with ACS among the list obtained from the record office. From this, 29 patients were excluded due to incomplete medical records for 30% of the variables, or due to referral or transfer from other hospitals for further management; 20 medical records were unable to be retrieved. A total of 147 patients were included in the final analysis.

The socio-demographic and clinical characteristics of young patients diagnosed with ACS are shown in Table 1. The mean (SD) age was 39.1 (4.97) years. The youngest patient was aged 21 years. The male to female ratio was 3:1, with Malays constituting the majority of the

Table 1. Socio-demographic characteristics of young patients diagnosed with ACS (n = 147)

	Frequency (%)	Range	Mean (SD)
Age (years)		21.0–44.0	39.10 (4.97)
Sex			
Male	110 (74.8)		
Female	37 (25.2)		
Race			
Malay	139 (94.6)		
Non-Malay	8 (5.4)		
Marital status			
Married	123 (83.7)		
Non-married	24 (16.3)		
Educational level			
None/Primary school	43 (29.3)		
Secondary school	49 (33.3)		
Tertiary education	55 (37.4)		
Occupation			
Housewife/Unemployed	23 (15.7)		
Self-employed	65 (44.2)		
Government/private sector	59 (40.1)		

studied patients (94.6%) compared with non-Malays (5.4%). Patients' highest education was as follows: none or primary education (29.3%), secondary education (33.3%) and tertiary education (37.4%). In terms of occupation, 15.7% were housewives or unemployed, 4.2% were self-employed and 40.1% were employees of government or private sectors.

Type of ACS Diagnosed in Young Patients

Out of 147 patients, 21.2% (31) were diagnosed as unstable angina (UA), 58.5% (86) as non-ST elevation myocardial infarction (NSTEMI) and 20.4% (30) as STEMI.

Prevalence of Risk Factors of ACS in Young Patients

Table 2 shows the risk factors associated with ACS among young patients. Dyslipidaemia was the most prevalent cardiovascular risk factor, present in 65.3% of patients. This was followed by diabetes mellitus (55%), hypertension (43.5%), current smoking (42.9%),

Table 2. Risk factors of young patients diagnosed with ACS (*n* = 147)

Risk factors	Frequency (%)
Smoking status	
Non-smoker	55 (37.4)
Ex-smoker	29 (19.7)
Current smoker	63 (42.9)
Co-morbidity*	
Dyslipidaemia	96 (65.3)
Hypertension	64 (43.5)
Heart disease	44 (29.9)
Obesity	40 (27.2)
Diabetes mellitus	38 (25.9)
Renal impairment	9 (6.1)
Stroke	8 (5.4)
Transient ischaemic attack	3 (2.0)
Peripheral vascular disease	2 (1.4)
Marfan's syndrome	1 (0.7)
Family history of coronary artery disease	63 (42.9)
Family history of premature death	21 (14.3)

*non-mutually exclusive

underlying heart diseases (29.9%) and obesity (27.2%). Family history of CAD was found in 42.9% of patients, and 14.3% had a family history of premature death.

Clinical Presentation of Young Patients with ACS

Table 3 shows the clinical presentation of young patients with ACS. The majority of patients had chest pain (76.9%); 49.6% each presented with this pain either in the left chest or retrosternal, respectively. Further, 28.6% had a previous similar history of presentation. In terms of the associated symptoms; 55.8% of patients

Table 3. Clinical presentation of young patients diagnosed with ACS (*n* = 147)

Clinical presentations	Frequency (%)
Chest pain	113 (76.9)
Previous similar history	42 (28.6)
Dyspnoea	82 (55.8)
Sweating	68 (46.3)
Palpitations	62 (42.2)
Nausea	36 (24.5)
Pain to left arm	32 (21.8)
Giddiness	19 (12.9)
Vomiting	18 (12.2)
Epigastric pain	17 (11.6)
Pain to jaw	11 (7.5)
Syncope	6 (4.1)
Tachycardia	32 (21.8)
Hypotension	6 (4.1)
Hypertension	53 (36.1)
Respiratory crackles	55 (37.4)
S3 gallop rhythm	6 (4.1)
Killip's classification	
I	85 (57.8)
II	40 (27.2)
III	13 (8.8)
IV	9 (6.2)
TIMI risk score	
0−2	111 (75.5)
3−4	21 (14.3)
5−7	12 (8.2)
> 7	3 (2.0)

had dyspnoea, followed by sweating (46.3%), palpitations (42.2%), nausea (24.5%), pain in the left arm (21.8%), giddiness (12.9%), vomiting (12.2%), jaw pain (7.5%) and syncope (4.1%).

During clinical examinations, it was found that 21.8% of patients were tachycardiac, 4.1% were hypotensive while 36.1% were hypertensive. Further, 37.4% had respiratory crackles and S3 gallop rhythm was found in 4.1% of patients. According to Killip's classification, 57.8% were Killip's class I, 27.2% were Killip's class II, 8.8% were Killip's class III and 6.1% were Killip's class IV.

For UA/NSTEMI, the TIMI risk scores of 0 to 2 were reported in 88.9% of patients, and scores of 3 to 4 were reported in 11.1% of patients, while there were no patients who scored 5 to 7. For STEMI, a wider range was observed. TIMI risk scores of 0 to 2 were reported in 20.7% of patients, scores of 3 to 4 in 27.6% of patients, scores of 5 to 7 in 41.3% of patients and scores of more than 7 in 10.4% of the patients.

Biochemical Markers, Stress Test and Echocardiography

Table 4 shows the biochemical markers, stress test and echocardiography results of the young patients with ACS. A troponin rapid test was conducted in 26 patients with positive results found in nine patients (65.4%). Serum lactate dehydrogenase (LDH) was measured in 139 patients; 88.5% of these had levels above 300 IU/L. Serum creatinine kinase (CK) was measured in 140 patients; 26.4% of these had levels above 400 IU/L. CK-MB measurement was performed in 21 patients; all had levels above 5 IU/L. Only 6.8% of patients had serum total cholesterol above 7.8 mmol/L, while 38.5% had serum high density lipid (HDL) level of less than 1.08 mmol/L, 14.4% had serum LDL more than 5.00 mmol/L and 20.4% had triglyceride more than 2.3 mmol/L. Only 31.2% of patients had random blood glucose above 7.0 mmol/L on arrival.

Table 4. Biochemical markers, stress test and echocardiography of young patients diagnosed with ACS ($n = 147$)

Test	n	Frequency (%)	Mean (SD)	Median (IQR)
Positive troponin	26	9 (34.6)		
LDH* (IU/L) > 300	139	123 (88.5)	811.99 (920.53)	83.00 (341.00, 773.00)
CK* (IU/L) > 400	140	37 (26.4)	682.51 (1292.76)	141.50 (87.75, 442.25)
CK-MB* (IU/L) > 5	21	21 (100)	105.84 (53.45)	41.00 (29.50, 100.00)
Total cholesterol (mmol/L) > 7.8	118	8 (6.8)	5.74 (1.43)	
HDL (mmol/L) < 1.08	96	37 (38.5)	1.17 (0.31)	
LDL (mmol/L) > 2.6	97	69 (71.1)	3.49 (1.34)	
Ratio LDL/HDL > 5	96	8 (8.3)		
Triglyceride (mmol/L) > 2.3	116	23 (20.4)	1.72 (0.97)	
Blood glucose (mmol/L) > 7.0	141	44 (31.2)	7.18 (3.60)	
Positive stress test	26		8 (30.8)	
Ejection fraction (%) > 50	93	19 (20.4)	59.74 (13.80)	

*non-normal distribution

Twenty-six patients underwent the stress test; eight patients returned a positive result (30.8%). Echocardiography was performed in 93 patients; 20.4% had an ejection fraction of less than 50%.

Pharmacological and Surgical Treatment

Table 5 shows the pharmacological treatment prescribed for young patients with ACS. The majority of patients received aspirin and statin (both 91.8%) and 86.4% received clopidogrel. Streptokinase were prescribed in 11.6% of patients while heparin was prescribed in 46.3% of patients and fondaparinux in 52.4% of patients. In total, 38.1% of patients received intravenous nitrates and 61.9% received oral nitrates. Beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitor (ACEI) and angiotensin II receptor antagonist (ARB) were prescribed in 50.3%, 36.7%, 74.1% and 2.0%, respectively.

Among the total sample, 39 patients (26.5%) underwent coronary angiography; 16 patients had percutaneous coronary intervention (PCI) and three patients underwent coronary artery bypass surgery (CABG).

Table 5. Pharmacological and surgical treatment of young patients diagnosed with ACS ($n = 147$)

Treatment*	Frequency (%)
Aspirin	135 (91.8)
Clopidogrel	127 (86.4)
Streptokinase	17 (11.6)
Heparin	68 (46.3)
Fondaparinux	77 (52.4)
Intravenous nitrates	56 (38.1)
Oral nitrates	91 (61.9)
Beta blocker	74 (50.3)
Calcium channel blocker	54 (36.7)
Statin	135 (91.8)
Angiotensin converting enzyme inhibitor	109 (74.1)
Angiotensin receptor blocker	3 (2.0)
Coronary angiography	39 (26.5)
Percutaneous coronary intervention	16 (41.0)
Coronary artery bypass surgery	3 (7.7)

*non-mutually exclusive

Complications of ACS in Young Patients

The results revealed that 73 (49.7%) patients had complication(s) associated with ACS while hospitalised. The most common complication was heart failure (35.4%), followed by arrhythmia (20.4%), pulmonary oedema and cardiogenic shock (both occurred in 13.6% of patients) and cardiac arrest (10.2%). The mortality rate during admission was 10.2%. Recurrent ischaemia and reinfarction occurred in 6.1% and 2.0% of patients, respectively. Table 6 shows the complications in young patients with ACS.

Table 6. Complications of young patients diagnosed with ACS ($n = 147$)

Complications	Frequency (%)
Present	73 (49.7)
Heart failure	52 (35.4)
Arrhythmia	30 (20.4)
Pulmonary oedema	20 (13.6)
Cardiogenic shock	20 (13.6)
Cardiac arrest	16 (10.9)
Mortality	15 (10.2)
Recurrent ischemia	9 (6.1)
Reinfarction	3 (2.0)

*non-mutually exclusive

Factors Associated with Complications of Young Patients with ACS

Table 7 shows factors associated with complications among young patients diagnosed with ACS. The significant factors associated with ACS complication in young patients were current smoking [AOR 4.03; 95% CI: 1.33, 12.23; *P*-value = 0.014], diabetic mellitus [AOR 3.03; 95% CI: 1.19, 7.71; *P*-value = 0.020], pharmacological treatments of fondaparinux [AOR 0.18; 95% CI: 0.08, 0.39; *P*-value < 0.001] and oral nitrates [AOR 0.18; 95% CI: 0.08, 0.42; *P*-value < 0.001].

Discussion

In the current study, 21.2% of patients were diagnosed as UA, 58.5% as NSTEMI and 20.4% as STEMI. In comparison, in the Thai ACS registry, 13.4% of patients were diagnosed as UA, 19.3% as NSTEMI and 67.3% as STEMI (3). Most of our patients had NSTEMI, in comparison with

Table 7. Factors associated with complications of young patients diagnosed with ACS ($n = 147$)

	Complication Frequency (%)		Crude OR[a] (95% CI)	Adjusted OR[b] (95% CI)	P-value
	Present $n = 73$	Absent $n = 74$			
Smoking status					
Non-smoker	27 (37.0)	28 (37.8)	1	1	
Ex-smoker	18 (24.6)	11 (14.9)	1.69 (0.68, 4.25)	1.62 (0.66, 3.96)	0.289
Current smoker	28 (38.4)	35 (47.3)	0.83 (0.40, 1.71)	4.03 (1.33, 12.23)	0.014
Diabetes					
No	47 (64.4)	62 (84.9)	1	1	
Yes	26 (35.6)	12 (15.1)	2.86 (1.31, 6.25)	3.03 (1.19, 7.71)	0.020
Fondaparinux					
No	48 (65.8)	22 (29.7)	1	1	
Yes	25 (34.2)	52 (70.3)	0.22 (0.11, 0.44)	0.18 (0.08, 0.39)	< 0.001
Oral nitrates					
No	41 (56.2)	15 (20.3)	1	1	
Yes	32 (43.8)	59 (79.7)	0.20 (0.10, 0.41)	0.18 (0.08, 0.42)	< 0.001

[a]Simple logistic regression
[b]Multiple logistic regression
The model reasonably fits well. Model assumptions are met. There are no interaction and multicollinearity problems

the GRACE and Euroheart studies, both of which showed that younger patients more frequently presented as STEMI. The GRACE registry reported that 46.5% of patients presented as STEMI, 25.7% presented as NSTEMI and 27.8% presented as UA (2). The Euroheart ACS survey revealed that, for people younger than 55 years, 56% of men and 44% of women presented as STEMI (11). This might be due to the occurrence of less severe coronary occlusion among the patients in our study. Alternatively, the classification might be affected by the fact that many of our cases did not have troponins and CK-MB performed. Furthermore, the sampling of our patients might not representative of young ACS in Malaysia.

The mean (SD) age of our patients was 39.1 (4.97) years. This is comparable to a study in Oman, among patients diagnosed with ACS aged less than 40 years, which showed a mean (SD) age of 36.0 (4.00) years (12). The youngest patient in our study was aged 21 years, as compared to the Thai ACS Registry whereby the youngest patient was 22.8 years old (3).

The male to female ratio in our study was 3:1. This was similar to other studies conducted in Thailand[3] and Switzerland (5). Although the incidence of acute myocardial infarction (AMI) increases sharply with age, women are less likely to experience AMI compared to men, at any given age, with a lag of approximately 9 to 10 years between the sexes (12). Comparatively, women tend to be 10 year older than men when they first experience an ischaemic episode (14).

A retrospective observational study of the pattern of ACS in the young people (40 years old or less) in a Dhaka military hospital showed that smoking was the most common risk factor; 64.1% of patients were smokers (15). In the current study, 37.4% of our patients were non-smokers, 42.9% were current smokers and 19.7% were ex-smokers.

Dyslipidaemia was the most prevalent cardiovascular risk factor in our study; observed in 65.3% of patients, followed by diabetes mellitus (55%), hypertension (43.5%) and underlying heart diseases (29.9%). Comparatively, in the GRACE registry, the figures were 39.7%, 12.1%, 34.4% and 40.7%, respectively (2). The high prevalence of dyslipidaemia and diabetes mellitus is probably related to the urbanisation of diet in developing countries. This fact was supported by the multicenter collaborative study of the International Clinical Epidemiology Network (INCLEN) which revealed that many developing countries had a higher than normal cholesterol level (16).

In the current study, the prevalence of obesity was 27.2%, which was lower compared to a study in Switzerland that reported that 57.8% of young ACS patients were overweight (5). In the past, it was believed that obesity was a disease of the developed world; however, more recently it has become evident that obesity is also a major health care burden in the developing world. The risk of developing CAD in obese patients is estimated to be about three times more than in those with normal body weight (16).

Family history of CAD was found in 42.9% of our patients, and 14.3% had a family history of premature death. In comparison, family history of CAD was found in 23.6% of young patients in Thailand (3) and 55.0% of young patients in Switzerland (5). The high prevalence of cardiovascular risk factors among our patients probably explains the presentation of ACS at a much younger age. It is likely that primary prevention plays an important role in controlling these risk factors.

The majority of our patients presented with Killip's class I (57.8%), in comparison to the GRACE registry, where 94.3% of patients presented with the same class (2). The reason for this might be related to the late presentation to hospital. In another study of young patients, most patients presented with Killip's class I or II, because Killip's class III and IV increased markedly with age (11).

Biomarkers play an important role in the diagnosis of ACS, especially in UA and NSTEMI. Cardiac troponin and CK are the most sensitive and specific markers of myocardial injury. Troponin measurements are now recognised as a valuable diagnostic tool; however, the availability of troponin testing is still very limited in developing countries (6). In our study, the mean total cholesterol level [5.74 (SD 1.43) mmol/L] was higher compared to that reported in the OASIS trial [5.1 (SD 2.0)] (17). The INCLEN study revealed that 20% of samples from seven developing countries had the mean total cholesterol level of more than 6.5 mmol/L (16). A study from Beijing attributed a significant rise in CAD mortality to each 1 mmol/L increase in total cholesterol (17). In addition, higher TG and lower HDL-cholesterol were observed in younger patients compared with older patients (19).

In our study, the percentage of patients who were prescribed the standard medication for ACS was similar to that reported by the Malaysian NCVD ACS registry (1) and the GRACE study (2). Reperfusion therapy is regarded as the standard therapy for most AMI patients with ST elevation. At present, thrombolytic therapy and primary angioplasty are regarded as viable option. The ENACT reported that 51% of patients with AMI received thrombolytic therapy, with a further 8% undergoing primary PCI. There was also a high prevalence of use of aspirin, heparin and beta-blockers (6). In the Malaysian NCVD ACS registry, streptokinase was solely used as a fibrinolytic agent; 70% of STEMI patients received fibrinolytic therapy. The reasons for not receiving fibrinolytic therapy included primary PCI, presentation after more than 12 hours, contraindication to streptokinase and refusal to treatment (1).

Statins were commonly prescribed for our patients. Statins can stabilise plaques in patients with atheromatous CHD, thereby improving outcomes and reducing recurrent events (4). Unfractionated heparin was prescribed more frequently to the younger group because less bleeding complications are seen in the younger patients compared to older patients (2). ACEI should be offered to all patients with left ventricular dysfunction as considerable benefits have been shown in this group of patients (4). GPIIb/IIIa has shown to lower ischaemic events in patients with ACS (3). Improvement in younger patients could be due to the fact that proven therapies are better implemented among younger patients (11).

Not many of our patients underwent coronary angiography; only 16 patients had PCI and three patients underwent CABG. In the Thai ACS registry, 64.3% underwent coronary angiography, 41.9% had PCI and 4% had CABG (3). The low percentage of patients who underwent a surgical procedure was due to the high refusal rate among the patients themselves. The opportunity for surgical intervention is also related to the availability of a cardiologist, cardiac intervention facilities and financial support.

Our study showed that 49.7% of patients had complication(s) associated with ACS while hospitalised. The most common complications among the patients were heart failure (35.4%) followed by arrhythmia (20.4%), pulmonary oedema and cardiogenic shock (13.6%). The rate of mortality during the admission was 10.2%. The rates of recurrent ischaemia and reinfarction were 6.1% and 2.0%, respectively. These findings are comparable with that of the Thai ACS registry in which 25.6% had heart failure, 9.2% had cardiogenic shock, 19.7% of cardiac

arrhythmia, 1.3% had stroke, 2.6% had major bleeding and the mortality rate was 7.4% (3). The GRACE study showed that only 6.1% had heart failure, 1.6% had cardiogenic shock, 2.3% had major bleeding, 0.6% had stroke and there was a mortality rate of 1.3% (2); these rates are low compared to our study. The favourable outcome among young ACS patients in the GRACE study, compared to our and Thailand studies, might be the consequence of typical clinical presentation giving rise to prompt treatment.

Our study found that current smokers had significantly four times the odds of having complications associated with ACS, compared to those who had never smoked, while there was no significant association between ex-smokers and ACS-related complications. In the Malaysian NCVD ACS Registry, current smokers and ex-smokers with ACS had significantly 2.5 and 3.3 times the odds, respectively, of in-hospital death, as compared to those who never smoke (1). The literature indicates that lifestyle changes play an important part in the management of ACS in young patients (4). Patients should be strongly advised to stop smoking. As smoking is a major modifiable risk factor, it should be aggressively targeted. Smoking cessation was shown to reduce CHD mortality by 36%, as compared to those who continued smoking (20).

Our study showed that diabetic patients had significantly three times the odds of having complications associated with ACS, compared to non-diabetic patients. The Malaysia NCVD ACS registry reported that diabetic patients with STEMI and NSTEMI/UA had significantly three to six times the odds of in-hospital death compared to non-diabetic patients (1). Intervention for diabetes mellitus should involve healthy dietary intake and exercise for a better control of glucose level. Dietary intervention has been shown to reduce cardiac event rates post STEMI (21). Although our study did not show a significant association between dyslipidaemia and ACS complications, clinical practice guidelines recommended that statin should be started soon after admission, and continued indefinitely. The target LDL cholesterol should be less than 2.0 mmol/L, and lowering even further (< 1.8 mmol/L) confers greater benefits (8). In addition, healthy dietary intake and exercise can also reduce dyslipidaemia.

Our study showed that the pharmacological treatments of fondaparinux and oral nitrates had protective effects on ACS-associated complications. Patients who received fondaparinux or oral nitrates were 92% less likely to have ACS-related complications compared to patients who did not receive the medication. A trial on fondaparinux was shown to reduce death or reinfarction at 30 days compared to unfractionated heparin. Sublingual GTN should be given as pre-hospital management and upon arrival at hospital if chest pain persists (8).

The Malaysia NCVD ACS registry showed that the predictors of in-hospital mortality in patients with STEMI were Killip class, TIMI risk score, diabetes mellitus, hypertension, cigarette smoking, family history of premature cardiovascular disease and dyslipidemia. While in NSTEMI/ UA, the predictors of in-hospital mortality were Killip class, smoking, diabetes mellitus and heart failure (1).

There were several limitations of our study. The population of young ACS patients in our institution was limited. Incomplete and non-retrieval medical records further contributed to the inadequate sample size for this study. In addition, this study was a retrospective record review that had the common disadvantages of secondary data with large amounts of missing information, variation of definitions of variables by different attending physicians and the assumption of unwritten variables as negative intakes or behaviours. Furthermore, our study was only a short-term study that evaluated in-hospital complications. This may be inadequate to describe the exact burden of premature coronary disease from a personal and societal point of view. Several emerging risk factors such as lipoprotein abnormalities, hypercoagulable states, elevated homocysteine levels, markers of inflammation and glycoprotein were not evaluated in this study.

In view of the above limitations, this study should be expanded to other hospitals in order to obtain more samples and to validate the findings in a wider population. With a larger sample size, the study could be divided according to each type of ACS (UA, NSTEMI and STEMI). This would be useful as each type might have different associated factors with regard to complications. A prospective study should be performed instead of a retrospective record review. A prospective study may demonstrate an appropriate temporal sequence between ACS and its related complications, and permit a direct calculation of incidence rates. Furthermore, it would allow examination of multiple outcomes. A study over a longer period and with follow-up

of patients is deemed beneficial as it may capture the true burden of premature coronary disease. Further, studies with more complete variables are required for a better understanding of the characteristics of ACS in young patients.

In conclusion, this retrospective record review of young ACS patients showed that there was a high prevalence of risk factors. The characteristics, treatment and complications associated with ACS in young patients in our institution were comparable with other studies. Smoking status and diabetes mellitus were significant risk factors, while pharmacological treatment with fondaparinux and oral nitrates were significant protective factors against complications associated with ACS in young patients aged less than 45 years.

Established modifiable cardiovascular risk factors such as dyslipidaemia, hypertension, heart disease, obesity, smoking and diabetes mellitus, in young patients, should be addressed via primary prevention. Such efforts require more assertive health education targeting younger populations. Screening at an earlier age among individuals with multiple risk factors may potentially reduce occurrence of ACS among people aged below 45 years.

Pharmacological treatments that show protective effects, such as fondaparinux and oral nitrates, and also other protective agents such as aspirin, beta blocker, ACEI, as found in the literature, should be prescribed to patients in order to reduce morbidity and mortality risks. More surgical interventions in young patients diagnosed with ACS should be carried out, as there are shown to produce good outcomes in this group of people. The difficulties in establishing required resources and financial support should be overcome through a multi-agency approach.

Conflict of Interest

The authors declare that they have no conflict of interests.

Authors' Contributions

Conception and design: NB
Analysis and interpretation of the data: C-MC'M
Drafting of the article: C-MC'M
Critical revision of the article for important intellectual content: NB
Final approval of the article: NB, C-MC'M
Provision of study materials or patients: NB, C-MC'M
Statistical expertise: NB, C-MC'M

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