Characteristics and short-term outcomes of young women with acute myocardial infarction in Malaysia: a retrospective analysis from the Malaysian National Cardiovascular Database registry

Padma Venkatasan, Yong Z Zubairi, Nur Lisa Zaharan, Wan Azman Wan Ahmad, Muhammad Imran Hafidz, Muhammad Dzafir Ismail, Mohd Firdaus Hadi, Norashikin Md Sari, Ahmad Syadi Mahmood Zuhdi

ABSTRACT

Objective Young women form a minority but an important group of patients with acute myocardial infarction (MI) as it can potentially cause devastating physical and socioeconomic impact. This study was aimed to investigate the characteristics and outcomes of young women with MI in Malaysia.

Design This is a retrospective analysis of women with ST-elevation MI (STEMI) and non-STEMI (NSTEMI) from 18 hospitals across Malaysia using the Malaysian National Cardiovascular Database registry–acute coronary syndrome (NCVD-ACS).

Participants Women patients diagnosed with acute MI from year 2006 to 2013 were identified and divided into young (age <45, n=292) and older women (age >45, n=5580).

Primary outcome measure Comparison of demographics, clinical characteristics and in-hospital management was performed between young and older women. In-hospital and 30-day all-cause mortality were examined.

Results Young women (mean age 39±4.68) made up 5% of women with MI and were predominantly of Malay ethnicities (53.8%). They have a higher tendency to present as STEMI compared with older women. Young women have significantly higher rates of family history of premature coronary artery disease (CAD) (20.5% vs 7.8%; p<0.0001). The prevalence of risk factors, such as hypertension, diabetes and dyslipidaemia was high in both groups. The primary reperfusion strategy was thrombolysis with no significant differences observed in the choice of intervention for both groups. Other than aspirin, rates of prescriptions for evidence-based medications were similar with >80% prescribed statins and aspirin. The all-cause mortality rates of young women were lower for both in-hospital and 30 days, especially in those with STEMI with adjusted mortality ratio to the older group, was 1.9:84.

Conclusion Young women with MI were over-represented by Malays and those with a family history of premature CAD. Preventive measures are needed to reduce cardiovascular risks in young women. Although in-hospital management was similar, short-term mortality outcomes favoured young compared with older women.

INTRODUCTION

Acute myocardial infarction (MI) is a predominantly male disease. Women, especially those of premenopausal age are at lesser risk of MI due to the protective effect of their sex hormones.1 2 In the Framingham Heart Study, the incidence of an MI in women aged 35 to 44 years over a 10-year follow-up was 5.2/1000 compared with 38.2/1000 in men of the same age group.3 In women, the highest incidence of MI occurred in those of 50 to 54 years old age group (23.1%).4 There was also evidence of a strong inverse association between age at menopause and coronary heart disease (CHD) risk.5

Malaysia is a unique multiethnic country in South East Asia, of which the prevalence of cardiovascular risk factors is rising6 due to changes in lifestyle. CHD is currently the second cause of mortality in women in this country (10.5%)7 in the year 2017; thus, there is a need to examine this issue in our women population for further improvement of service. In a study that examined Malaysian...
patients with the acute coronary syndrome (ACS) from the year 2006 to 2010 (n=13591), it was found that nearly a quarter (24%) of patients were women and they had more risk factors, less likely to undergo intervention and had higher mortality compared with men. Although the incidence is rather low, the impact of MI on young women’s childbearing years, their active lifestyle and their socioeconomic status can be devastating. An earlier study between 2006 and 2008 showed that 1.9% of Malaysian patients with ACS were young women in the reproductive age group (20 to less than 40 years old). Young women showed a higher postinfarction mortality in hospital and up to 1 year after discharge in comparison to men (4.23% vs 2.21%, p=0.005). There is a shortage of studies that have attempted to explore the characteristics and clinical outcomes of young women in this population compared with older women, and hence more information is required for this particular group. This study used data from the Malaysian National Cardiovascular Database registry–acute coronary syndrome (NCVD-ACS) to examine the clinical characteristics of young women with MI and their outcomes compared with older women of over 45 years old. This registry is part of the NCVD registry whereby 18 hospitals across Malaysia recorded information on patients with cardiovascular diseases from the year 2006 till current. This database provided valuable information on cardiovascular disease in this region of the world.

**METHODS**

**Study subjects and data collection**

The Malaysian NCVD-ACS registry is a prospective registry sponsored by the Ministry of Health, Malaysia (MoH) and cosponsored by the National Heart Association of Malaysia (NHAM). This registry included information on demographic information, cardiovascular diagnosis, comorbidities, family history, in-hospital management and on-discharge medications for adult patients in Malaysia who presented with cardiovascular disease at the participating hospitals. The details of the registry have been described in detail elsewhere. Anonymous patient data were obtained from this registry to identify women patients admitted with ST-elevation MI (STEMI) and non-ST elevation MI (NSTEMI) from the year of 2006 to 2013. Patients who were identified were divided into two categories: women aged 45 and below, also considered as young women similar to the definition used in the PRIMVAC Register (n=292) and women above the age of 45 (n=5580). Those above the age of 45 will be known as older women. Sample size calculation was not included in the analysis as the frame

| Table 1 Baseline characteristics, risk factors and comorbidities of young (age ≤45) and older (age >45) women with acute MI in the Malaysian NCVD-ACS registry from the year 2006 until the year 2013 |
|-------------------------------------------------|------------------|------------------|----------|
| **Age** (Year) | Young women (n=292) | Older women (n=5580) | P value |
| N,% or mean±SD | N,% or mean±SD | N,% or mean±SD |<0.001 |
| Ethnicity | | | |
| Malay | 157 (53.8%) | 2626 (47.1%) | |
| Chinese | 38 (13.0%) | 1312 (23.5%) | <0.001 |
| Indian | 68 (23.3%) | 1347 (24.1%) | |
| Others | 29 (9.9%) | 295 (5.3%) | |
| Risk factors | | | |
| Smoker (active/ex) | 27 (9.6%) | 533 (10.2%) | 0.738 |
| Dyslipidaemia | 84 (37.8%) | 2032 (46.7%) | 0.010 |
| Hypertension | 143 (57.7%) | 4321 (82.8%) | <0.001 |
| Diabetes mellitus | 136 (55.7%) | 3261 (64.2%) | 0.007 |
| Family history of premature CAD | 60 (20.5%) | 437 (7.8%) | <0.001 |
| Comorbidities | | | |
| Cerebrovascular disease | 8 (3.2%) | 271 (5.6%) | 0.114 |
| Peripheral vascular disease | 4 (1.6%) | 53 (1.1%) | 0.452 |
| Chronic lung disease | 4 (1.6%) | 157 (3.2%) | 0.159 |
| Congestive heart failure | 20 (6.8%) | 534 (9.6%) | 0.144 |
| Chronic renal failure | 13 (5.3%) | 633 (13.0%) | <0.001 |

All p values were calculated using the χ² test unless stated; *t-test.

CAD, coronary artery disease.
of the study was chosen from the objective of studying women with two categories of age. All data were extracted from the original raw data.

Variables obtained from the database for the purpose of this study were demographic variables such as age, ethnicity (Malay, Chinese, Indian and others), risk factors such as smoking status, diabetes, hypertension, dyslipidaemia and family history of premature coronary artery disease (CAD), comorbidities such as cerebrovascular disease, peripheral vascular disease, chronic lung disease, congestive heart failure and chronic renal failure, ACS diagnosis (STEMI, N-STEMI), type of Killip classes (I-IV), cardiac enzymes (peak troponin I, creatine kinase (CK), CK-MB) and left ventricular ejection fraction (LVEF). The in-hospital intervention included were thrombolysis, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) surgery. Evidence-based medications were defined as classes of drugs which carried outcome benefit and recommended in clinical guidelines13 which include antiplatelets (aspirin and ADP-receptor antagonist), angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), lipid-lowering medications (statins only) and beta-adrenoceptor blockers (beta-blockers).

Table 2 Clinical presentations of young (age ≤45) and older (age >45) women with acute MI in the Malaysian NCVD-ACS registry from the year 2006 until year 2013

| Diagnosis                      | Young women (n=292) | Older women (n=5580) | P value |
|--------------------------------|---------------------|----------------------|---------|
|                                | N, % or mean±SD     | N, % or mean±SD      |         |
| STEMI                          | 188 (64.4%)         | 2622 (47.0%)         | <0.001  |
| NSTEMI                         | 104 (35.6%)         | 2958 (53.0%)         |         |
| Killip Class                   |                     |                      |         |
| Killip 1                       | 167 (73.6%)         | 2404 (57.4%)         |         |
| Killip 2                       | 29 (12.8%)          | 1079 (25.8%)         | <0.001  |
| Killip 3                       | 7 (3.1%)            | 330 (7.9%)           |         |
| Killip 4                       | 24 (10.6%)          | 374 (8.9%)           |         |
| Cardiac enzymes*              |                     |                      |         |
| Peak troponin I (ng/ml)        | 10.28±14.30         | 6.39±12.90           | 0.001   |
| -Median (IQR)                  | 0.41 (0.05, 11.04)  | 0.19 (0.02, 2.06)    | <0.001  |
| Creatine kinase (CK) (unit)    | 865.83±1070.70      | 802.06±1173.80       | 0.01    |
| CK-MB (unit)                   | 63.10±71.0          | 63.55±95.72          | 0.12    |
| Left ventricular ejection fraction *(LVEF) (%) | 47.04±17.76 | 46.76±12.87 | 0.05 |

Note: All p values were calculated using the \( \chi^2 \) test unless stated; *t-test.
value of 1. All analyses were conducted using SPSS statistical software (V21, IBM SPSS Statistics, USA).

**Patient and public involvement**

There was no patient or public participation in the development of this study’s research question and outcome. All data were obtained retrospectively from the Malaysian NCVD-ACS. Result of this study will not be disseminated to study participants.

**RESULTS**

**Baseline characteristics and clinical presentation**

Young women made up only 5% (n=292) of the total women patients who presented with ACS in the Malaysian NCVD registry (n=5872). Malay ethnicity group was more predominant in young women (table 1). Young women have less cardiovascular risk factors compared with older women except for a premature family history of CAD. Young women presented more with STEMI and Killip 1 class compared with older women, as shown in table 2. Although CK and troponin levels were significantly higher in young women, the LVEF was similar between the two groups.

**In-hospital invasive coronary revascularisation and evidence-based pharmacotherapy**

Intravenous thrombolysis was the mainstay of reperfusion therapy in both groups (table 3). No significant difference was found between young and older women in terms of intravenous thrombolysis. However, the door-to-needle time for young women was slightly longer. The rate of PCI was similar. More than 80% of women patients were prescribed aspirin and statins. Aspirin was prescribed more in young women while the rest of the medications were similarly prescribed in both groups. The length of hospital stay was significantly shorter for young women.

**Early clinical outcomes of in-hospital and 30-day all-cause mortality**

The in-hospital and 30-day all-cause mortality outcomes are presented in tables 4 and 5, respectively. Mortality rates between the two groups differed significantly in favour of young women. Young women had significantly lower in-hospital and 30-day all-cause mortality across all strata of ACS type. They showed a more favourable outcome compared with older women with an adjusted mortality risk ratio of 1: 9.84, respectively. The gap in mortality rates of young women to the older group significantly increased at 30 days in the NSTEMI subgroup. The adjusted mortality risk for older women increased from 5.58 at in-hospital to 9.084 at 30 days.

**DISCUSSION**

This study describes the clinical characteristics and outcome of young women with acute MI in the Malaysian population. Young women (aged 45 years or less)
made up only 5% of the women patients in our nationwide registry. They have a higher tendency to present as STEMI compared with older women, although they have lower rates of cardiovascular risk factor profile. Interestingly, young women have significantly higher rates of family history of premature CAD. The primary reperfusion strategy for STEMI remained pharmacological with intravenous thrombolytic agents instead of the preferred catheter-based approach. No significant differences were observed in the choice of intervention for both groups. Other than aspirin, the rates of prescriptions for evidence-based medications were similar. The in-hospital mortality and mortality at 30 days were lower for the younger patients, especially in those with STEMI.

Traditionally, the impact of CAD on women has always been underestimated as CAD is often believed to be a ‘man’s disease.’ Changes in cultural and socio-economic structures through recent years see young women projecting themselves as frontliners in Malaysia’s workforce. Majority of Malaysian women have income-generating jobs and remain as central figures in their children care and upbringing. Thus, to suffer from a debilitating illness is equally devastating for women as it is for men. The low prevalence of young women in this study is consistent with other previous reports. Future studies should explore how to further model this finding for the projection of future disease burden in the country.

There seemed to be a Malay ethnic predilection in young women with MI. Malaysian women in the general population comprise mainly of Malays (54.9%) followed by Chinese (24.1%), Indian (7.4%) and others (20.0%). There was also an over-representation of the Indian ethnicity in both young and older women. This disproportionately high number of Indian ethnics among MI cohort has also been reported previously in Singapore, a neighbouring Asian country with demography quite similar to the Malaysian population. Racial tendency

### Table 4 Comparison of in-hospital mortality between young (age ≤45) and older (age >45) Malaysian women presented as unadjusted and adjusted risk ratio (RR) with 95% CI

|                         | Number of patients | Deaths n (%) | Unadjusted risk ratio (95% CI) | P value | Adjusted risk ratio* (95% CI) | P value |
|-------------------------|--------------------|--------------|-------------------------------|---------|-------------------------------|---------|
| **All patients (n=5761)** |                    |              |                               |         |                               |         |
| Young women             | 287                | 15 (5.2%)    | Reference                      | Reference |
| Older women             | 5474               | 660 (12.1%)  | 6.23 (4.90 to 7.56)           | <0.001  | 6.58 (5.01 to 7.94)           | <0.001  |
| **STEMI (n=2748)**      |                    |              |                               |         |                               |         |
| Young women             | 185                | 12 (6.5%)    | Reference                      | Reference |
| Older women             | 2563               | 411 (16.0%)  | 9.45 (8.21 to 10.43)          | 0.001   | 9.84 (8.74 to 10.92)          | <0.001  |
| **NSTEMI (n=3013)**     |                    |              |                               |         |                               |         |
| Young women             | 102                | 3 (2.9%)     | Reference                      | Reference |
| Older women             | 2911               | 249 (8.6%)   | 5.21 (4.56 to 6.87)           | 0.044   | 5.58 (4.97 to 7.02)           | 0.023   |

*Adjusted for age, ethnicity, dyslipidaemia, hypertension, diabetes, family history of premature CAD, chronic renal failure, Killip class, door to needle time, aspirin, statin and PCI.

### Table 5 Comparison of 30-day mortality between young (age ≤45) and older (age >45) Malaysian women presented as unadjusted and adjusted risk ratio (RR) with 95% CI

|                         | Number of patients | Deaths n (%) | Unadjusted risk ratio (95% CI) | P value | Adjusted risk ratio* (95% CI) | P value |
|-------------------------|--------------------|--------------|-------------------------------|---------|-------------------------------|---------|
| **All patients (n=5872)** |                    |              |                               |         |                               |         |
| Young women             | 292                | 18 (6.2%)    | Reference                      | Reference |
| Older women             | 5580               | 853 (15.3)   | 8.01 (7.01 to 9.56)           | <0.001  | 8.57 (7.85 to 10.12)          | <0.001  |
| **STEMI (n=2810)**      |                    |              |                               |         |                               |         |
| Young women             | 188                | 15 (8.0%)    | Reference                      | Reference |
| Older women             | 2622               | 490 (18.7%)  | 9.05 (8.09 to 11.34)          | <0.001  | 9.87 (9.01 to 12.93)          | <0.001  |
| **NSTEMI (n=3062)**     |                    |              |                               |         |                               |         |
| Young women             | 102                | 3 (2.9%)     | Reference                      | Reference |
| Older women             | 2958               | 363 (12.3%)  | 8.95 (7.41 to 9.21)           | 0.004   | 9.08 (7.98 to 10.82)          | 0.002   |

*Adjusted for age, ethnicity, dyslipidaemia, hypertension, diabetes, family history of premature CAD, chronic renal failure, Killip Class, door to needle time, aspirin, statin and PCI.
in young women with MI could be related to our finding of a higher rate of family history of premature CAD. Genetic backgrounds may play an essential role in MI predisposition in young women population, and thus, molecular studies should be undertaken to explore this further.

The rates of conventional risk factors in young women in our study were higher than the national prevalence of the diseases. Of those young women with MI, 58% have hypertension compared with 32% national prevalence, 55% have diabetes (12% national prevalence) and 38% have dyslipidemia (7% national population) (NHMS III). 17 The low prevalence of smoking in our young women (10%) is consistent with the finding among young women with acute MI in Singapore. 18 This pattern is different from the Western population as cigarette smoking is reported as the predominant risk factor among young women. 5–11 We do not have information in the registry on emerging non-traditional risk factors of MI in women such as hypertensive disorders in pregnancy, gestational diabetes, preterm delivery and depression 20 and, thus, these factors were not considered in this study. However, our findings suggest that despite the possibility of other unique variables which may contribute to the incidence of acute MI in young women, traditional risk factors remain important.

The majority of acute MI patients would present to hospitals that are not equipped for acute angiography/angioplasty and subsequently would receive thrombolysis. 21 In this study, more than half of young women received thrombolysis (69.2%) as compared with 43% of young women 50 years and below in New Jersey. 22 PCI and CABG were less preferred among young women in this study. As young Malaysian women had a lower mortality rate as compared with the older group, they showed better prognosis after fibrinolytic therapy. 23 Evidence-based cardiovascular medicines for secondary prevention are recommended as secondary preventative cardiovascular therapy to reduce the risk of recurrent events. 24 Some studies have shown that women were less likely to receive appropriate pharmacotherapy after MI. 24 The rate of prescribing of antiplatelet and statins in both young and older women in this population is satisfactory and adhere to international guidelines. The prescribing of ACEIs/ARBs and beta-blockers in our women were consistent with findings from previous studies on Malaysian population with MI 25 and may reflect the prescribing preference in this country.

The door to needle time for young women is longer than for older women. This finding may reflect the relative lack of clinical suspicion of acute MI in young women, and hence, the longer time is taken to achieve a diagnosis and initiate treatment. However, the mortality for both in-hospital and at 30 days was higher in older women. Thus, it seems that age itself is a significant independent predictor of mortality in women with MI. More worryingly, the short-term mortality from MI for Malaysian is higher than Western counterparts, 26 and this may require measures to improve diagnosis and management strategies in this population.

This study used data from a well-maintained national cardiovascular registry and can provide information on cardiovascular disease in this region of the world. As this study used registry-based data, there are inherent limitations. There were other non-participating hospitals in the country, and thus there may be selection bias. There is a possibility of intercentre variation, which is presented in the online supplementary figure 1a,b. The study sample size is rather small, as our objective was focused on young women. MI in young women could be underestimated as young women who presented with symptoms of MI may not be investigated as such. There may be information that is not captured in the database, such as underlying diagnosis of spontaneous coronary artery dissection (SCAD) and drug use or abuse in young women that could possibly influence management and outcome. LVEF was used as estimates of patients’ functional status as information on New York Heart Association classification were incomplete. The in-hospital and 30-day mortality outcomes were measures of short-term clinical outcome. Unfortunately, at the moment, data were not available for long-term outcome in this registry.

CONCLUSION

Young women are a minority group of patients with MI in our nationwide cardiovascular registry. Ethnicity and family history of premature cardiovascular disease may play a role in the predisposition of MI in these young women patients. Young women with MI do have higher rates of cardiovascular risk factors compared with the national population, and this needs to be addressed in preventative strategies. The short-term mortality outcomes favoured young compared with older women in both STEMI and NSTEMI.

Author affiliations
1Department of Medicine, University of Malaya Faculty of Medicine, Kuala Lumpur, Malaysia
2Foundation Studies in Science, Universiti Malaya, Kuala Lumpur, Wilayah Persekutuan, Malaysia
3Department of Pharmacology, University of Malaya Medical Centre, Kuala Lumpur, Wilayah Persekutuan, Malaysia
4Cardiology Unit, Department of Medicine, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

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