Original Article

Ethnic Differences and Trends in ST-Segment Elevation Myocardial Infarction Incidence and Mortality in a Multi-Ethnic Population

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Abstract

Introduction: This study aimed to compare the incidence and mortality of ST-segment elevation myocardial infarction (STEMI) across the 3 main ethnic groups in Singapore, determine if there is any improvement in trends over the years and postulate the reasons underlying the ethnic disparity. Materials and Methods: This study consisted of 16,983 consecutive STEMI patients who sought treatment from all public hospitals in Singapore from 2007 to 2014. Results: Compared to the Chinese (58 per 100,000 population in 2014), higher STEMI incidence rate was consistently observed in the Malays (114 per 100,000 population) and Indians (126 per 100,000 population). While the incidence rate for the Chinese and Indians remained relatively stable over the years, the incidence rate for the Malays rose slightly. Relative to the Indians (30-day and 1-year all-cause mortality at 9% and 13%, respectively, in 2014), higher 30-day and 1-year all-cause mortality rates were observed in the Chinese (15% and 21%) and Malays (13% and 18%). Besides the Malays having higher adjusted 1-year all-cause mortality, all other ethnic disparities in 30-day and 1-year mortality risk were attenuated after adjusting for demographics, comorbidities and primary percutaneous coronary intervention. Conclusion: It is important to continuously evaluate the effectiveness of existing programmes and practices as the aetiology of STEMI evolves with time, and to strike a balance between prevention and management efforts as well as between improving the outcome of "poorer" and "better" STEMI survivors with finite resources.

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Key words: Chinese, Indian, Malay, STEMI

Introduction

Ischaemic heart disease (IHD) is the world's leading cause of death and is responsible for more than 8 million deaths each year.[1] Mirroring global trends, IHD has been among the top 3 causes of death for Singapore residents in recent years.[2] With Singapore's ageing population, coupled with the high prevalence of cardiovascular (CV) risk factors in the community,[3] the incidence and mortality of acute myocardial infarction (AMI) are expected to rise in future. Hence, it is imperative to identify at-risk subpopulations so that targeted prevention and management programmes can be implemented to improve outcomes.

ST-segment elevation myocardial infarction (STEMI), a type of AMI, is one of the most acute and severe presentation of IHD. It contributes significantly to CV mortality and morbidity. While the risk of getting AMI is increased by smoking, physical inactivity, poor nutrition, obesity, high blood cholesterol, high blood pressure, diabetes and metabolic syndrome,[4] the risk of dying after AMI is affected by the frailty of patient, severity of AMI, time of first treatment and process of continuous management in the short- and long-term.[5,6,7] Prior studies have shown ethnic differences in patients diagnosed with AMI in terms of presentation, risk factors, coronary vessel

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diameters, prognoses and outcomes.[8,9,10,11,12,13] Specifically, South Asians were found to have high risk for mortality, complications and recurrent AMI. These studies were generally conducted in Caucasian-majority settings and South Asians were generally treated as a single group. Asia houses some 60% of the world's population and as a region, has the fastest population growth rate. It has been increasingly recognised that even among subtypes of Asians, ethnicity is emerging as an important determinant of acute coronary syndrome outcomes.[14]

Singapore is a small, densely populated multi-ethnic country in Asia with 3 main ethnic groups—Chinese, Malay and Indian. Besides having a universally accessible healthcare system, Singapore has a good infrastructure for disease surveillance. These characteristics make Singapore suitable as a natural population laboratory to study the interaction between ethnicity and diseases. As the risk profile of each ethnic group differs due to varying genetic composition, dietary preference and lifestyle behaviour, the type and prevalence of CV incidence and mortality risk factors in each ethnic group are expected to differ.

This study aimed to compare the incidence and mortality of STEMI across the 3 main ethnic groups in Singapore, determine if there is any improvement in trends over the years and postulate the reasons underlying the ethnic disparity.

Materials and Methods

Setting

Singapore is a highly urbanised island city-state located in Southeast Asia with a population of 5.6 million, a land area of 719.1 square kilometres and a population density of 7797 persons per square kilometres in 2016.[15] Singapore has a gross domestic product of 402,160 million dollars (at 2010 market prices) and a life expectancy of 82.9 years in 2016.[16] Singapore has a mixed healthcare system,[17] where the public healthcare system is funded through a system of compulsory savings, subsidies and price controls.[18] There are 5 public hospitals that are located geographically evenly in Singapore which provide around-the-clock emergency percutaneous coronary intervention (PCI).[19,20] The composition of the 3 main ethnic groups in Singapore in 2016 was: 74% Chinese, 13% Malays and 9% Indians.[15] Specifically, the Singapore population comprises primarily third- and fourth-generation migrants of Han Chinese, Malay (Austronesian) and Indian (South Asian) descent.

Data Sources

The study population was obtained from the Singapore Myocardial Infarction Registry (SMIR). The SMIR is a state-funded nationwide registry managed by the National Registry of Diseases Office.[21] It captures epidemiological data on AMI cases diagnosed in all public and private hospitals and a small number of out-of-hospital AMI deaths certified by medical practitioners. All public hospitals provide notification of AMI cases to the SMIR since 2007, while legislation mandated notification from all hospitals (including private hospitals) since 2012. About 98% of all AMI cases in Singapore are managed by the public hospitals. The SMIR receives AMI case notification from 1) Hospital Inpatient Discharge Summary, 2) cardiac biomarker lists from all hospitals, 3) Mediclaim lists, 4) Casemix and Subvention lists from the Ministry of Health, and 5) death lists from the Ministry of Home Affairs, based on International Classification of Diseases 9th (ICD-9) Clinical Modification code 410 and ICD-10 Australian Modification codes I21 and I22. A team of registry coordinators—who are trained nurses—would review each case to verify that it is indeed an AMI. Detailed patient data for each AMI case will then be captured from the electronic medical records and physical casenotes. The same data extraction method is applied to all hospitals. To ensure that the data captured are accurate and consistent, yearly internal audit is performed by the SMIR to ensure inter-rater reliability of at least 95%.

Case-level procedural data related to PCI were obtained from the Singapore Cardiac Databank, which captures data related to CV diseases and procedures delivered in the public hospitals.[22]

Aggregated data on the number of Singapore residents were obtained from the Singapore Department of Statistics, which releases mid-year resident population estimates annually.

Patient-level death data were obtained from the Death Registry under the purview of the Ministry of Home Affairs.

Study Population

All patients with STEMI in January 2007 to December 2014 were included. Only STEMI (rather than all AMI) were included in this study as STEMI often results from a primary CV event rather than secondary to another disease such as sepsis. A small number of patients (~2%) who presented to the private hospitals were excluded as data from the private hospitals were available only from 2012 onwards.

Outcomes of Interest

The outcomes of interest in this study are: STEMI incidence, 30-day mortality and 1-year mortality from all-cause, CV and non-CV deaths. All-cause death was selected as it encompasses the overall mortality and can be ascertained without adjudication. Mortality was further classified into CV and non-CV to differentiate whether the death is likely resultant of STEMI or other diseases. CV mortality was defined as death due primarily to a CV disease such as IHD, heart failure, arrhythmia, valvular heart disease, pericardial disease, myocarditis, pulmonary

hypertension or stroke.[23] The 30-day mortality was used to assess immediate outcome of STEMI, while 1-year mortality was for longer-term assessment. As the reporting of death is mandatory for all Singapore residents and the vital statuses of study population (patients with STEMI in January 2007 to December 2014) were matched until 30 April 2016 (a date that is beyond 1 year from the last AMI case included in this study), no patient was lost to follow-up for all mortality outcomes.

Ethics Approval

The Centralised Institutional Review Board of Singapore General Hospital (CIRB Reference: 2014/130/C) granted ethics approval with waiver of patient consent for this study, which utilised anonymised registry data.

Statistical Analysis

Differences in patients' demographics, comorbidities, procedural characteristics, medications and in-hospital events across the ethnic groups were compared using Kruskal-Wallis rank test for numeric variables and chi-square test for categorical variables.

Yearly STEMI incidence rates were plotted for the 3 ethnic groups to compare their trends over the years. Annual incidence rate was calculated by dividing the number of STEMI episodes by the number of Singapore residents in each year.

Yearly 30-day and 1-year all-cause, CV and non-CV mortality rates were plotted for the 3 ethnic groups to compare their trends over the years. Annual 30-day and 1-year mortality rates were calculated by dividing the number of STEMI patients who died within 30 days and 1 year, respectively, from the onset date of STEMI by the number of STEMI patients in each year. Kaplan-Meier curves were plotted for the 3 ethnic groups to compare their cumulative mortality rate within 30 days and 1 year after STEMI.

The relationship between ethnic group and mortality was examined using Cox regression. Demographics (age, gender), comorbidities (history of hypertension, history of diabetes, history of hyperlipidaemia, history of AMI/PCI/coronary artery bypass graft, smoking status, body mass index, heart failure on admission, serum creatinine on admission) and primary PCI were adjusted sequentially in multivariable Cox regression. These factors were selected based on their clinical and statistical significance to mortality. For CV mortality, competing risk from non-CV death was accounted in Cox regression. The reverse was applied to non-CV mortality.

The data used in this study were mostly completed and missing data were mostly missing at random. To maintain the data in its original form, missing data were dropped from analyses through case deletion without any imputation. Of the 16,983 consecutive patients in the univariable analyses, 13,500 (79%) were also in the multivariable analyses after dropping those with missing data. Sensitivity analysis done on the 13,500 patients that remained in the multivariable models found similar ethnic disparities in patients' characteristics.

All statistical analyses were done using STATA SE (version 13) software. All reported *P* values were two-sided and $P < 0.05$ was considered statistically significant.

Results

Study Population

Of the 16,983 consecutive patients in this study, 11,056 (65.1%) were Chinese, 3399 (20.0%) Malays and 2528 (14.9%) Indians. Table 1 shows the ethnic differences in demographics, comorbidities, procedural characteristics, medications and in-hospital events. Median age at STEMI was oldest for the Chinese (62 years) and they had the highest proportion of patients with history of hypertension (59.1%). Median serum creatinine on admission was highest for the Malays (96 μmol/L) and they had the highest proportion of patients who smoked (67.9%) and with high body mass index (73.2%). The Indians had the highest proportion of patients with history of diabetes (44.1%), hyperlipidaemia (51.3%) and AMI/PCI/coronary artery bypass graft (21.5%). The proportion of Indians who received primary PCI (70.1%) and pharmacotherapy was higher than the Chinese and Malays. Median door-to-balloon time was longest for the Indians (70 minutes), but median symptom-to-balloon time was longest for the Malays (195 minutes). While in-hospital arrhythmia was most common among the Chinese (28.7%), in-hospital acute renal failure was most common among the Malays (8.6%). The proportion of Chinese and Malays experiencing heart failure during hospitalisation were similar at 15%, but higher than the Indians (12.8%).

Incidence

STEMI incidence rate for the Malays and Indians were consistently higher than the Chinese from 2007 to 2014 (Fig. 1). While the incidence rate for the Chinese (62 and 58 per 100,000 population in 2007 and 2014, respectively) and Indians (122 and 126 per 100,000 population in 2007 and 2014, respectively) remained relatively stable over the years, the incidence rate for the Malays rose slightly from 97 per 100,000 population in 2007 to 114 per 100,000 population in 2014.

30-Day Mortality

All-cause and CV mortality rate for the Chinese (all-cause mortality 17%, CV mortality 14%) and Malays (all-cause

Table 1. Demographics, Comorbidities, Procedural Characteristics, Medications, In-Hospital Events and Mortality of the Study Population

	Chinese (n = 11,056)	Malays (n = 3399)	Indians (n = 2528)	*P* Value
Demographics				
Age in years, median (IQR)	62 (54 − 74)	58 (51 − 67)	56 (49 − 64)	<0.001
Male, n (%)	8549 (77.3)	2741 (80.6)	2037 (80.6)	<0.001
Comorbidities				
History of hypertension, n (%)	6466 (59.1)	1815 (54.0)	1324 (52.8)	<0.001
History of diabetes, n (%)	3131 (28.6)	1242 (37.0)	1108 (44.1)	<0.001
History of hyperlipidaemia, n (%)	5127 (46.9)	1522 (45.3)	1286 (51.3)	<0.001
History of AMI/PCI/CABG, n (%)	1526 (13.9)	575 (17.1)	541 (21.5)	<0.001
Current/former smoker, n (%)	5899 (55.1)	2238 (67.9)	1446 (58.5)	<0.001
Body mass index >23 kg/m^2, n (%)	5305 (60.0)	2028 (73.2)	1489 (69.4)	<0.001
Heart failure on admission, n (%)	2365 (21.6)	721 (21.4)	501 (19.9)	0.180
Serum creatinine on admission in μmol/L, median (IQR)	93 (77 − 118)	96 (80 − 121)	88 (74 − 104)	<0.001
Procedural Characteristics				
Reperfusion therapy, n (%)	6948 (62.8)	2233 (65.7)	1852 (73.3)	<0.001
Primary PCI, n (%)	6585 (59.6)	2140 (63.0)	1773 (70.1)	<0.001
Door-to-balloon in minutes, median (IQR)	68 (51 − 91)	67 (51 − 90)	70 (53 − 95)	0.001
Symptom-to-balloon in minutes, median (IQR)	188 (122 − 315)	195 (129 − 333)	189 (120 − 321)	0.028
Number of diseased vessels, n (%)				0.003
Normal or minor coronary artery disease	15 (0.3)	3 (0.2)	5 (0.4)	
Single-vessel disease	1907 (36.4)	632 (36.6)	573 (42.0)	
Double-vessel disease	1757 (33.5)	545 (31.5)	421 (30.8)	
Triple-vessel disease	1561 (29.8)	548 (31.7)	366 (26.8)	
Number of lesions intervened, n (%)				0.673
Single	5191 (95.0)	1705 (94.6)	1366 (95.2)	
Multiple	272 (5.0)	98 (5.4)	69 (4.8)	
Lesion intervened, n (%)				
Left main	117 (2.1)	38 (2.1)	22 (1.5)	0.337
Left anterior descending	2786 (51.0)	916 (50.8)	678 (47.3)	0.037
Left circumflex	627 (11.5)	205 (11.4)	244 (17.0)	<0.001
Right coronary artery	2225 (40.7)	755 (41.9)	569 (39.7)	0.437
Pre-PCI TIMI flow (%)				0.382
0	3481 (72.5)	1168 (71.4)	902 (71.3)	
I	314 (6.5)	129 (7.9)	85 (6.7)	
II	479 (10.0)	158 (9.7)	119 (9.4)	
III	531 (11.0)	180 (11.0)	160 (12.6)	
Post-TIMI flow >II and resolution of ST-segment elevation >50%, n (%)	5338 (97.8)	1761 (97.7)	1403 (97.9)	0.902
Use of stent, n (%)				
Bare metal stent	3461 (63.4)	1128 (62.6)	847 (59.0)	0.011
Drug eluting stent	1557 (28.5)	518 (28.7)	420 (29.3)	0.848
Bioresorbable vascular scaffold	66 (1.2)	30 (1.7)	15 (1.1)	0.228
Medications Given Within 24 hours from Onset				
Aspirin, n (%)	9860 (89.2)	3086 (90.8)	2342 (92.6)	<0.001
Beta blocker, n (%)	5393 (48.8)	1651 (48.6)	1391 (55.0)	<0.001
Other antiplatelets, n (%)	9839 (89.0)	3129 (92.1)	2389 (94.5)	<0.001

ACEI: Angiotensin converting enzyme inhibitor; AMI: Acute myocardial infarction; ARB: Angiotensin receptor blocker; CABG: Coronary artery bypass graft; CV: Cardiovascular; IQR: Interquartile range; PCI: Percutaneous coronary intervention; TIMI: Thrombolysis in myocardial infarct

Table 1. Demographics, Comorbidities, Procedural Characteristics, Medications, In-Hospital Events and Mortality of the Study Population (Cont'd)

	Chinese (n = 11,056)	Malays (n = 3399)	Indians (n = 2528)	*P* Value
Medications Given at Discharge				
Aspirin, n (%)	8639 (93.0)	2719 (92.6)	2160 (94.9)	0.002
Beta blocker, n (%)	7938 (85.4)	2547 (86.8)	1985 (87.2)	0.035
ACEI/ARB, n (%)	6696 (72.1)	2084 (71.0)	1704 (74.9)	0.006
Lipid-lowering therapy/statin, n (%)	8842 (95.2)	2811 (95.8)	2203 (96.8)	0.003
Other antiplatelets, n (%)	8480 (91.3)	2756 (93.9)	2159 (94.9)	<0.001
Events During Hospitalisation				
Heart failure, n (%)	1668 (15.3)	511 (15.2)	322 (12.8)	0.007
Arrhythmia, n (%)	3141 (28.7)	901 (26.8)	592 (23.6)	<0.001
Complete heart block, n (%)	420 (3.8)	134 (4.0)	81 (3.2)	0.266
Acute renal failure, n (%)	796 (7.3)	290 (8.6)	148 (5.9)	<0.001
Stroke, n (%)	164 (1.5)	67 (2.0)	34 (1.4)	0.082
Left ventricular ejection fraction <50%, n (%)	6247 (66.2)	1995 (66.6)	1436 (63.7)	0.054
Mortality				
All-cause death within 30 days, n (%)	1848 (16.7)	490 (14.4)	253 (10.0)	<0.001
CV death within 30 days, n (%)	1557 (14.1)	431 (12.7)	229 (9.1)	<0.001
Non-CV death within 30 days, n (%)	291 (2.6)	59 (1.7)	24 (1.0)	<0.001
All-cause death within 1 year, n (%)	2454 (22.2)	674 (19.8)	352 (13.9)	<0.001
CV death within 1 year, n (%)	1876 (17.0)	543 (16.0)	287 (11.4)	<0.001
Non-CV death within 1 year, n (%)	578 (5.2)	131 (3.9)	65 (2.6)	<0.001

ACEI: Angiotensin converting enzyme inhibitor; AMI: Acute myocardial infarction; ARB: Angiotensin receptor blocker; CABG: Coronary artery bypass graft; CV: Cardiovascular; IQR: Interquartile range; PCI: Percutaneous coronary intervention; TIMI: Thrombolysis in myocardial infarct

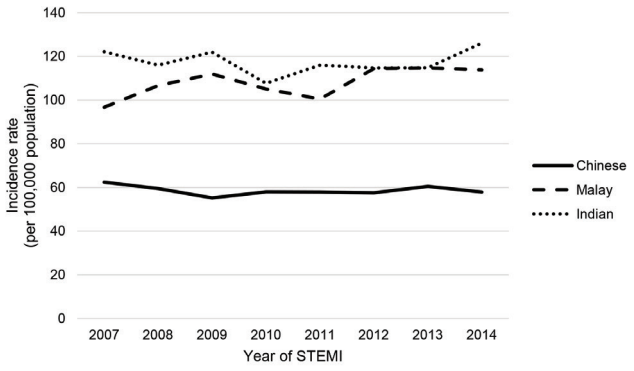

Fig. 1. Graph showing the incidence rate across the years. STEMI: ST-segment elevation myocardial infarction.

mortality 14%, CV mortality 13%) were consistently higher than the Indians (all-cause mortality 10%, CV mortality 9%) from 2007 to 2014, although the mortality rate did not show any clear upward or downward trend over the years for the 3 ethnic groups (Fig. 2). Cumulative mortality rate after STEMI was highest for the Chinese and lowest for the Indians (Fig. 3). The number of CV deaths was about 5-, 7- and 9-fold of non-CV deaths among the Chinese, Malays and Indians, respectively (Table 1). Compared to the Chinese, the unadjusted risk of all-cause death after STEMI was significantly lower for the Malays (hazard ratio [HR] 0.84, 95% confidence interval [CI] 0.75-0.94) and Indians (HR 0.58, 95% CI 0.50-0.67) (Table 2). The lower unadjusted mortality risk among the Malays and Indians was also observed for CV deaths (Malays: HR 0.89, 95% CI 0.78-1.00; Indians: HR 0.63, 95% CI 0.54-0.74) and non-CV deaths (Malays: HR 0.64, 95% CI 0.47-0.86; Indians: HR 0.39, 95% CI 0.26-0.59). Notably, the mortality risks among the Malays exceeded the Chinese—albeit not significantly higher—after adjusting for demographics, comorbidities and primary PCI. For the Indians, their adjusted mortality risks were similar to the Chinese.

One-Year Mortality

All-cause and CV mortality rates for the Chinese (all-cause mortality 22%, CV mortality 17%) and Malays (all-cause mortality 20%, CV mortality 16%) were consistently higher than the Indians (all-cause mortality 14%, CV mortality 11%) from 2007 to 2014, although the mortality rate did not show any clear upward or downward trend over the years for the 3 ethnic groups (Fig. 2). Cumulative mortality rate after STEMI was highest for the Chinese and lowest for the Indians (Fig. 3). The number of CV deaths was more than non-CV deaths, but not more than 5-fold across the 3 ethnic groups (Table 1). Compared to the Chinese, the unadjusted risk of all-cause death after STEMI was significantly lower

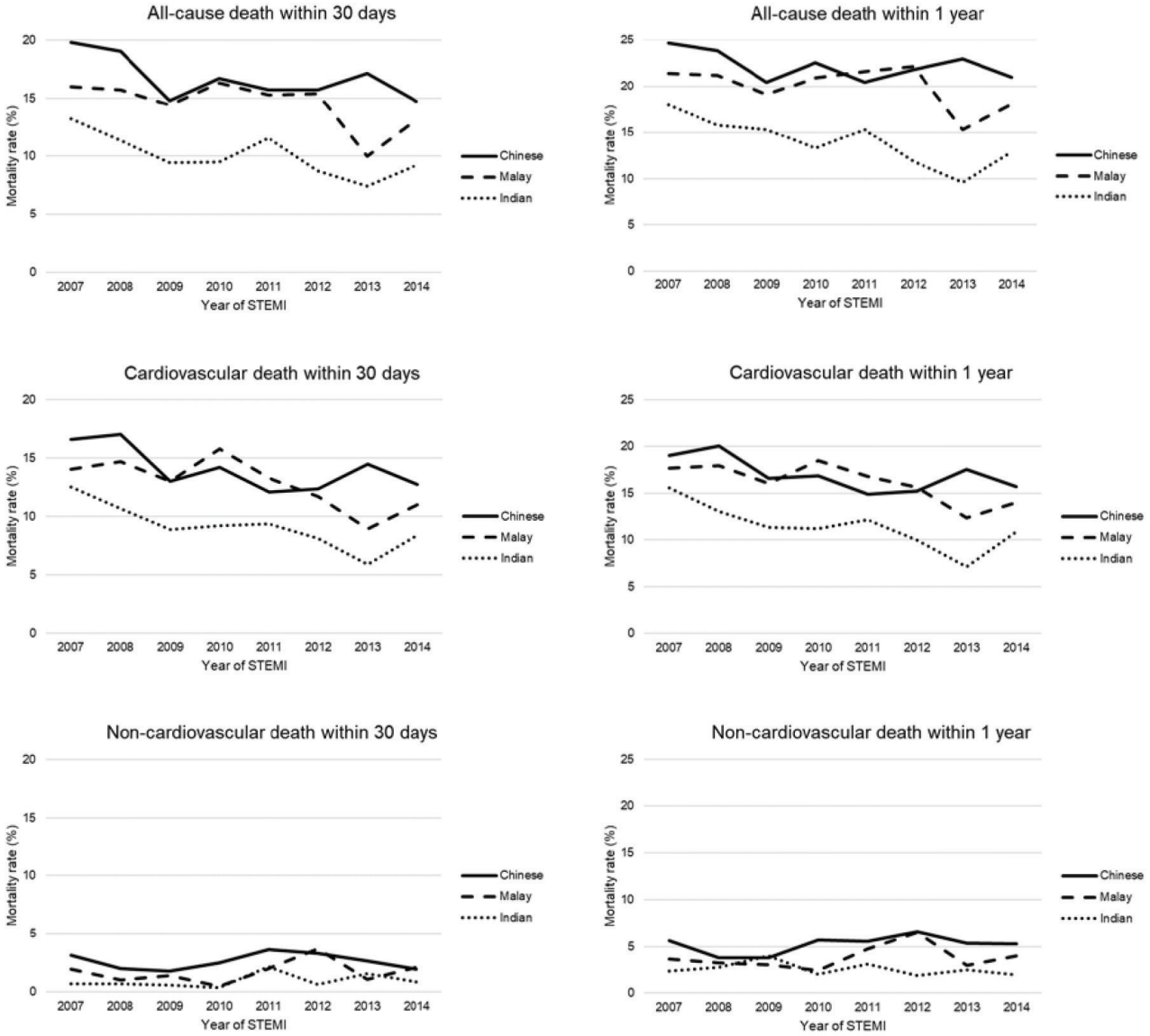

Fig. 2. Graphs showing the mortality rate across the years. STEMI: ST-segment elevation myocardial infarction.

for the Malays (HR 0.87, 95% CI 0.80-0.96) and Indians (HR 0.60, 95% CI 0.53-0.68) (Table 2). The lower unadjusted 1-year mortality risk among the Malays and Indians were also observed for CV deaths (Malays: HR 0.94, 95% CI 0.84-1.04; Indians: HR 0.66, 95% CI 0.57-0.75) and non-CV deaths (Malays: HR 0.72, 95% CI 0.60-0.88; Indians: HR 0.50, 95% CI 0.39-0.65). The 1-year all-cause and CV mortality risks for the Malays became significantly higher than the Chinese after adjusting for demographics, comorbidities and primary PCI, although the adjusted risk of non-CV death for the Malays was similar to the Chinese. For the Indians, their adjusted mortality risks were similar to the Chinese.

Discussion

Ethnic disparity in STEMI incidence rate was observed in the general population as well as in 30-day and 1-year mortality rates among STEMI patients. Higher STEMI incidence rate was consistently observed in Malays and Indians. While the incidence rate for Chinese and Indians remained relatively stable over the years, the incidence rate for Malays rose slightly. Higher 30-day and 1-year mortality rates were observed in Chinese and Malays for all-cause and CV deaths, but not non-CV deaths. Cumulative mortality rate within 30 days and 1 year after STEMI was highest for the Chinese and lowest for the Indians. Of the deaths within 30 days after STEMI, Indians had the highest

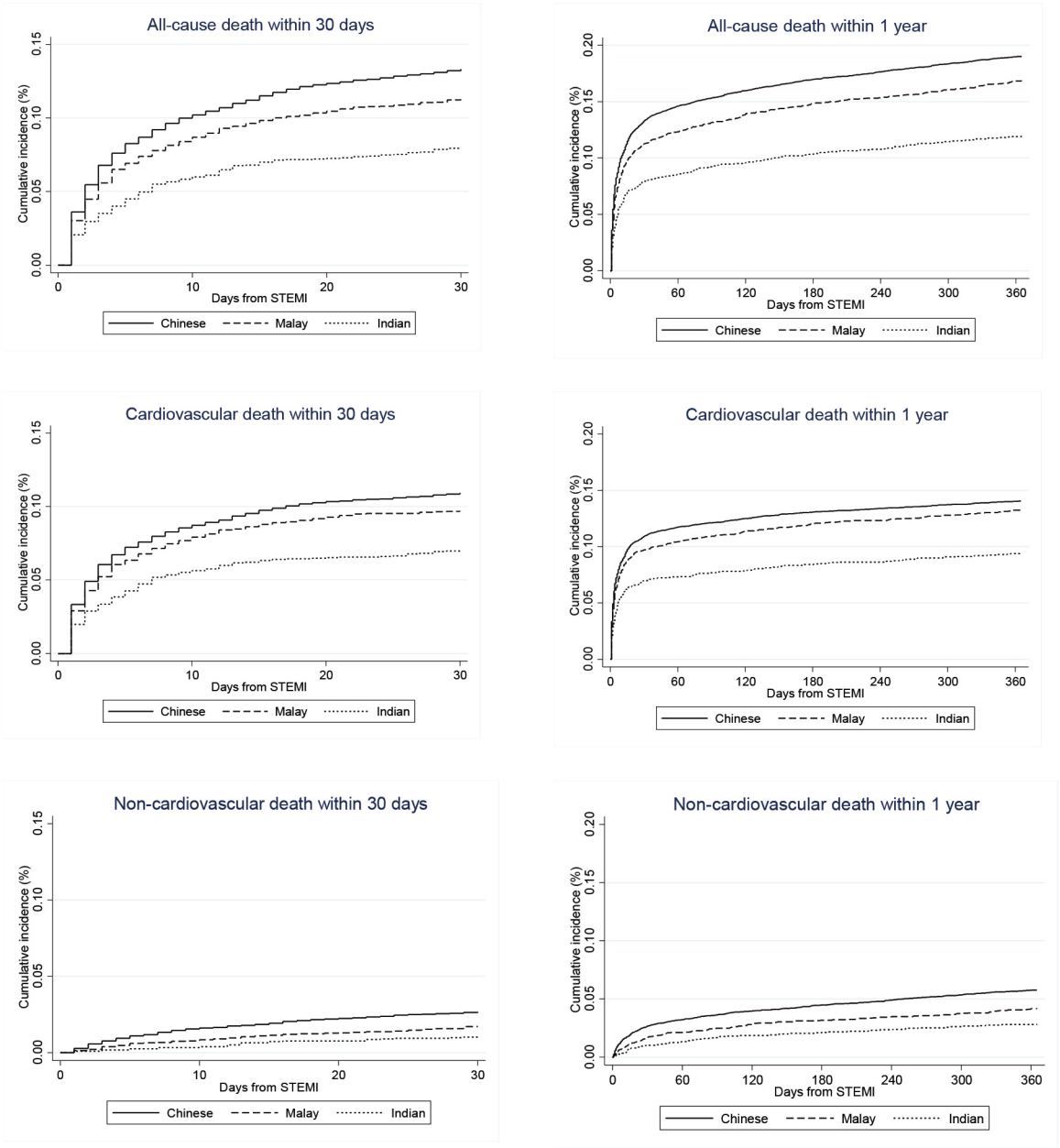

Fig. 3. Graphs showing the cumulative mortality rate after ST-segment elevation myocardial infarction (STEMI).

proportion of CV deaths. Besides Malays having higher adjusted 1-year all-cause and CV mortality risk, all other ethnic disparities in 30-day and 1-year mortality risk were attenuated after adjusting for demographics, comorbidities and primary PCI.

The findings in this study corroborated with that from existing literature. In a similar study by Mak et al, higher AMI incidence was observed among Malays and Indians from 1991 to 1999.[24] The 28-day and 1-year age-adjusted mortality rates were lowest for Indians and highest for Malays. The study, however, did not adjust for other factors besides age and gender. In a more recent study by Gao et al, ethnic disparities were found to be wider in 30-day and 10-year CV mortality than non-CV mortality in patients with AMI from 2000 to 2005.[25] Our study complements theirs with the inclusion of analyses on incidence and intermediate 1-year mortality.

Incidence

The National Health Surveys and National Nutrition Surveys done by the Ministry of Health and Health Promotion Board, respectively, found that the Malays had the highest prevalence of hypertension, hyperlipidaemia, smoking, obesity, physical inactivity and low consumption

Table 2. Hazard Ratios (95% Confidence Interval) for Mortality

	Chinese (n = 11,056)	Malays (n = 3399)	Indians (n = 2528)
All-cause death within 30 days			
Model 1	1.00	0.84 (0.75 − 0.94)	0.58 (0.50 − 0.67)
Model 2	1.00	1.16 (1.04 − 1.31)	0.89 (0.76 − 1.03)
Model 3	1.00	1.06 (0.90 − 1.23)	0.92 (0.76 − 1.12)
Model 4	1.00	1.03 (0.88 − 1.21)	0.97 (0.80 − 1.18)
CV death within 30 days			
Model 1	1.00	0.89 (0.78 − 1.00)	0.63 (0.54 − 0.74)
Model 2	1.00	1.22 (1.08 − 1.38)	0.96 (0.81 − 1.12)
Model 3	1.00	1.10 (0.92 − 1.31)	0.97 (0.79 − 1.20)
Model 4	1.00	1.08 (0.91 − 1.29)	1.01 (0.82 − 1.24)
Non-CV death within 30 days			
Model 1	1.00	0.64 (0.47 − 0.86)	0.39 (0.26 − 0.59)
Model 2	1.00	0.91 (0.68 − 1.23)	0.61 (0.40 − 0.93)
Model 3	1.00	0.93 (0.64 − 1.36)	0.73 (0.44 − 1.21)
Model 4	1.00	0.88 (0.61 − 1.29)	0.82 (0.50 − 1.35)
All-cause death within 1 year			
Model 1	1.00	0.87 (0.80 − 0.96)	0.60 (0.53 − 0.68)
Model 2	1.00	1.24 (1.13 − 1.36)	0.94 (0.83 − 1.06)
Model 3	1.00	1.16 (1.03 − 1.31)	0.92 (0.79 − 1.08)
Model 4	1.00	1.14 (1.01 − 1.28)	0.98 (0.84 − 1.14)
CV death within 1 year			
Model 1	1.00	0.94 (0.84 − 1.04)	0.66 (0.57 − 0.75)
Model 2	1.00	1.30 (1.17 − 1.44)	0.99 (0.87 − 1.14)
Model 3	1.00	1.19 (1.03 − 1.38)	0.99 (0.83 − 1.18)
Model 4	1.00	1.18 (1.02 − 1.36)	1.03 (0.87 − 1.23)
Non-CV death within 1 year			
Model 1	1.00	0.72 (0.60 − 0.88)	0.50 (0.39 − 0.65)
Model 2	1.00	1.06 (0.87 − 1.29)	0.81 (0.62 − 1.05)
Model 3	1.00	1.11 (0.88 − 1.40)	0.76 (0.56 − 1.04)
Model 4	1.00	1.07 (0.85 − 1.35)	0.82 (0.60 − 1.13)

CV: Cardiovascular
Chinese is the reference group.
Model 1 consists of: ethnic group.
Model 2 consists of: variable in Model 1, demographics (age, gender).
Model 3 consists of: variables in Model 2, comorbidities (history of hypertension, history of diabetes, history of hyperlipidaemia, history of acute myocardial infarction/percutaneous coronary intervention/ coronary artery bypass graft, smoking status, body mass index, heart failure on admission, serum creatinine on admission).
Model 4 consists of: variables in Model 3, primary PCI.

of fruits and vegetables which are common risk factors of STEMI.[3,4,26] Their prevalence of diabetes, hypertension, smoking, obesity, physical inactivity and low consumption of fruits and vegetables increased over the years.[3,26] Malays were also least likely to go for regular health screening for hypertension, diabetes and hyperlipidaemia.[3] Although the prevalence of hypertension and hyperlipidaemia among Indians were lower than the Chinese, the prevalence of diabetes among Indians was higher than the Chinese.[3] Furthermore, Indians have ethnic-specific risk for coronary artery disease.[27,28] The high prevalence of STEMI risk factors among Malays and the combination of STEMI risk factors in the backdrop of genetic predisposition to heart diseases among Indians are likely reasons for their higher STEMI incidence rate relative to the Chinese.

Thirty-Day Mortality

Unadjusted all-cause and CV mortality among Chinese was evidently higher, but there was no significant ethnic difference in mortality risk after adjusting for demographics, comorbidities and primary PCI. This suggests that the ethnic differences in all-cause and CV mortality could be

largely explained by their differences in demographics, comorbidities and primary PCI. Older age at STEMI, accompanied by hypertension and other comorbidities (not restricted to those captured in this study), predisposed the Chinese to higher mortality risk.[29] These factors could have also led to the lower proportion of Chinese receiving treatment (primary PCI with pharmacotherapy) recommended by the American Heart Association[30] and European Society of Cardiology.[31]

One-Year Mortality

Unadjusted all-cause and CV mortality among the Chinese was evidently higher. The mortality risk was significantly higher among Malays, but not significantly lower among Indians after adjusting for demographics, comorbidities and primary PCI.

The lower unadjusted mortality risk among Malays than the Chinese could be due to Malays having lower prevalence of mortality risk factors in terms of quantity and/or impact. However, after adjusting for demographics, comorbidities and primary PCI, Malays could have fared worse among the mortality risk factors (not restricted to those captured in this study) that were not adjusted in the models, thereby pushing up their adjusted mortality risk to be higher than the Chinese. Although the proportion of Malays who underwent primary PCI was higher than the Chinese, the median symptom-to-balloon time for Malays was longer than the Chinese. Longer symptom-to-balloon time could potentially compromise the benefit of primary PCI.[32,33] Moreover, despite significantly higher proportion of Malays having triple-vessel disease, the proportion of them having multiple lesions intervened was not significantly higher. Incomplete revascularisation of non-culprit lesions in non-infarct-related artery could have also contributed to the higher adjusted mortality risk among Malays.[34]

Higher rates of primary PCI and pharmacotherapy are associated with lower rates of in-hospital event, which could have conferred lower unadjusted mortality risk among Indians.[29] The higher rates of primary PCI and pharmacotherapy among Indians also implied that they might be physically fitter at the onset of STEMI, rendering them eligible for primary PCI and pharmacotherapy.

Implications

The findings in this study revealed different risk profiles across the 3 ethnic groups. For the Chinese, the high mortality rate was largely attributed to their older age at STEMI with accompanying comorbidities that impeded their treatment options. More could be done to reduce treatment-risk paradox in the hope of narrowing the ethnic gap, although the trend of Chinese having the highest mortality rate is expected to persist in future.

For the Malays, the high STEMI incidence and mortality rate were largely due to their high prevalence of STEMI and mortality risk factors. More intensive prevention and management programmes are warranted to improve the health status of Malays before and after STEMI. For example, the smoking cessation programme organised by the Health Promotion Board has a special Ramadan edition with intensive targeted outreach to Malay smokers during their fasting month. In addition, chronic disease screening and health workshops that equip participants with practical ways of keeping active and eating wisely are also offered at no charge to religious institutions such as mosques. This makes early detection and management of chronic diseases—which is crucial in preventing STEMI—more accessible for the ethnic groups. Efforts to improve the survival of STEMI patients are ongoing. Besides having primary PCI as the main modality of reperfusion therapy, more strategically located acute and community hospitals have been built. Twelve-lead electrocardiogram machines that allow wireless transmission of data en-route to hospital and mechanical cardiopulmonary resuscitation devices that deliver consistent and quality chest compressions have been installed in all public emergency ambulances.[35] However, these population-based management efforts are not ethnic-specific. Mirroring the ethnic-specific prevention programmes that are already in place in the community, more risk stratification and targeted management programmes, which take into account socio-cultural sensitivities could be implemented in the clinical setting as well.

For the Indians, although their mortality rate was low, most of their deaths within 30 days after STEMI was CV-related and might be preventable with closer monitoring to ensure adequate medical compliance and cardiac rehabilitation.

Strengths and Limitations

As the study population is an unselected pool of STEMI patients with data that were consistently captured across all hospitals and close to complete coverage of all AMI cases, the findings in this study are representative of the entire STEMI cohort in Singapore. However, this study also has its limitations.

Firstly, there is some ambiguity in the classification of ethnicity for the offspring of inter-ethnic marriages. Ethnicity is currently classified based on the race that a person most identified with (socially) as reflected in the unique identity card that every Singapore resident holds, rather than his/her (biologically) dominant genetic makeup. There is no official national statistic on the number of people of mixed-ethnicity, but using the number of inter-ethnic marriages in Singapore as a proxy, about 1 in 5 people are estimated to be of mixed-ethnicity.[15] The impact of mixed-ethnicity on our findings remains to be answered and

it would be interesting for future studies to focus on this group of people and investigate how their disease patterns vary from people of pure-ethnicity. Secondly, as the study population is limited to only STEMI patients without any control, a more in-depth analysis on the association between STEMI incidence and its risk factors could not be done. Nonetheless, triangulation of our findings with existing national surveys had been done in an attempt to explain the incidence trends. Thirdly, postdischarge factors related to mortality such as medication compliance and cardiac rehabilitation—which are not available at population-level—could not be accounted in this study. Fourthly, as there is time lag between behavioural change and STEMI development, it is not feasible to evaluate the impact of existing ethnic-specific prevention programmes at this juncture. If proven to be successful, such programmes can pave the path for tailored lifestyle intervention programmes to be extended to more religious institutions as a viable scale-up plan in future.

Conclusion

Ethnic differences in STEMI incidence and mortality persist in the contemporary cohort despite the implementation of ethnic-specific prevention programmes, improvement in prehospital facilities and rise in usage of primary PCI and pharmacotherapy in recent years. It will be useful to continuously evaluate the effectiveness of existing programmes and practices as the aetiology of STEMI evolves with time. It is also crucial to strike a balance between prevention and management efforts, as well as between improving the outcome of "poorer" and "better" STEMI survivors with finite resources.

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REFERENCES

1. World Health Organization. The Top 10 Causes of Death. 2017. Available at: http://www.who.int/mediacentre/factsheets/fs310/en/. Accessed on 21 March 2017.
2. Ministry of Health, Singapore. Principal Causes of Death. 2014. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Principal_Causes_of_Death.html. Accessed on 21 March 2017.
3. Ministry of Health, Singapore. National Health Survey 2010. Available at: https://www.moh.gov.sg/content/moh_web/home/Publications/Reports/2011/national_health_survey2010.html. Accessed on 21 March 2017.
4. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364:937-52.
5. Writing Group Members, Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, et al. Heart disease and stroke statistics−2016 update: a report from the American Heart Association. Circulation 2016;133:e38-360.
6. Chan MY, Becker RC, Sim LL, Tan V, Lee CH, Low AF, et al. Reperfusion strategy and mortality in ST-elevation myocardial infarction among patients with and without impaired renal function. Ann Acad Med Singapore 2010;39:179-84.
7. Ong SH, Lim VY, Chang BC, Lingamanaicker J, Tan CH, Goh YS, et al. Three-year experience of primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction in a hospital without on-site cardiac surgery. Ann Acad Med Singapore 2009;38:1085-9.
8. Albarak J, Nijjar APK, Aymong E, Wang H, Quan H, Khan NA. Outcomes in young South Asian Canadians after acute myocardial infarction. Can J Cardiol 2012;28:178-83.
9. Gasevic D, Khan NA, Qian H, Karim S, Simkus G, Quan H, et al. Outcomes following percutaneous coronary intervention and coronary artery bypass grafting surgery in Chinese, South Asian and White patients with acute myocardial infarction: administrative data analysis. BMC Cardiovasc Disord 2013;13:121.
10. Khan NA, Grubisic M, Hemmelgarn B, Humphries K, King KM, Quan H. Outcomes after acute myocardial infarction in South Asian, Chinese, and White patients. Circulation 2010;122:1570-7.
11. Toor IS, Jaumdally R, Lip GYH, Pagano D, Dimitri W, Millane T, et al. Differences between South Asians and White Europeans in five year outcome following percutaneous coronary intervention. Int J Clin Pract 2011;65:1259-66.
12. Krishnamurthy A, Keeble C, Burton-Wood N, Somers K, Anderson M, Harland C, et al. Clinical outcomes following primary percutaneous coronary intervention for ST-elevation myocardial infarction according to sex and race. Eur Heart J Acute Cardiovasc Care 2017;2048872617735803.
13. Bhopal R, Unwin N, White M, Yallop J, Walker L, Alberti KG, et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi, and European origin populations: cross sectional study. BMJ 1999;319:215-20.
14. Chan MY, Du X, Eccleston D, Ma C, Mohanan PP, Ogita M, et al. Acute coronary syndrome in the Asia-Pacific region. Int J Cardiol 2016;202:861-9.
15. Department of Statistics, Singapore. Population Trends 2016. 2016. Available at: http://www.singstat.gov.sg/docs/default-source/default-document-library/publications/publications_and_papers/population_and_population_structure/population2016.pdf. Accessed on 21 March 2017.
16. Department of Statistics, Singapore. Singapore in Figures 2017. 2017. Available at: http://www.singstat.gov.sg/docs/default-source/default-document-library/publications/publications_and_papers/reference/sif2017.pdf. Accessed on 9 February 2018.
17. Lim J. Myth or Magic: The Singapore Healthcare System. Singapore: Select Publishing, 2013. p. 6.
18. World Health Organization. The World Health Report 2000: Health Systems: Improving Performance. Available at: http://www.who.int/whr/2000/en/whr00_en.pdf?ua=1. Accessed on 21 March 2017.
19. Ho AFW, Chew D, Wong TH, Ng YY, Pek PP, Lim SH, et al. Prehospital trauma care in Singapore. Prehosp Emerg Care 2015;19:409-15.
20. Ho AF, Loy EY, Pek PP, Wah W, Tan TX, Liu N, et al. Emergency medical services utilization among patients with ST-segment elevation myocardial infarction: observations from the Singapore Myocardial Infarction Registry. Prehosp Emerg Care 2016;20: 454-61.

21. National Registry of Diseases Office, Singapore. Singapore Myocardial Infarction Registry Annual Report 2007-2017. Available at: https://www.nrdo.gov.sg/publications/ami. Accessed on 20 September 2018.
22. Singapore Cardiac Data Bank, Singapore. Clinical Sciences and Statistics Core. Available at: https://www.nhcs.com.sg/nhris/Pages/Research/ResearchCores/ClinicalSciencesandStatisticsCore.aspx. Accessed on 20 September 2018.
23. Hicks KA, Mahaffey KW, Mehran R, Nissen SE, Wiviott SD, Dunn B, et al. 2017 cardiovascular and stroke endpoint definitions for clinical trials. Circulation 2018;137:961-72.
24. Mak KH, Chia KS, Kark JD, Chua T, Tan C, Foong BH, et al. Ethnic differences in acute myocardial infarction in Singapore. Eur Heart J 2003;24:151-60.
25. Gao F, Lam CSP, Yeo KK, Machin D, de Carvalho LP, Sim LL, et al. Influence of ethnicity, age, and time on sex disparities in long-term cause-specific mortality after acute myocardial infarction. J Am Heart Assoc 2016;5:e003760.
26. Health Promotion Board, Singapore. National Nutrition Survey 2010. Available at: https://www.hpb.gov.sg/docs/default-source/pdf/nns-2010-report.pdf?sfvrsn=18e3f172_2. Accessed on 21 March 2017.
27. Sasidhar M V, Reddy S, Naik A, Naik S. Genetics of coronary artery disease – a clinician's perspective. Indian Heart J 2014;66:663-71.
28. Heng CK, Low PS, Saha N. Variations in the promoter region of the apolipoprotein A-1 gene influence plasma lipoprotein(a) levels in Asian Indian neonates from Singapore. Pediatr Res 2001;49:514-8.
29. Rasoul S, Ottervanger JP, de Boer MJ, Dambrink JH, Hoorntje JC, Marcel Gosselink AT, et al. Predictors of 30-day and 1-year mortality after primary percutaneous coronary intervention for ST-elevation myocardial infarction. Coron Artery Dis 2009;20:415-21.
30. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). Circulation 2004;110:588-636.
31. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018;39:119-77.
32. De Luca G, Suryapranata H, Zijlstra F, van 't Hof AW, Hoorntje JC, Gosselink AT, et al. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol 2003;42:991-7.
33. Kireyev D, Tan HC, Poh KK. Management of acute ST-elevation myocardial infarction: reperfusion options. Ann Acad Med Singapore 2010;39:927-33.
34. Varenhorst C, Hasvold P, Johansson S, Janzon M, Albertsson P, Leosdottir M, et al. Culprit and non-culprit recurrent ischemic events in patients with myocardial infarction: data from SWEDEHEART (Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies). J Am Heart Assoc 2018;7:e007174.
35. Ong MEH, Wong ASL, Seet CM, Teo SG, Lim BL, Ong PJ, et al. Nationwide improvement of door-to-balloon times in patients with acute ST-segment elevation myocardial infarction requiring primary percutaneous coronary intervention with out-of-hospital 12-lead ECG recording and transmission. Ann Emerg Med 2013;61:339-47.