# Ethnic Differences in Utilization of Invasive Cardiac Procedures and in Long-Term Survival Following Acute Myocardial Infarction

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#### Summary

*Background:* Ethnic differences in coronary mortality have been documented, and South Asians from the Indian subcontinent are particularly vulnerable.

Hypothesis: This study sought to determine whether there was a difference in the utilization of invasive cardiac procedures and long-term mortality in survivors of myocardial infarction (MI) among Chinese, Malays, and South Asians in Singapore.

Methods: All MI events in the country were identified and defined by the Singapore Myocardial Infarction Register, which uses modified procedures of the World Health Organization MONICA Project. Information on utilization of coronary angiography, coronary angioplasty, coronary artery bypass graft, and survival was obtained by data linkage with national billing and death registries. Hazard ratios (HR) were calculated using the Cox proportional hazards model with adjustment for baseline characteristics.

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*Results:* From 1991 to 1999, there were 10,294 patients who survived  $\geq 3$  days of MI. Of these, 40.6% underwent coronary angiography and 16.5% a revascularization procedure  $\leq 28$  days. Malays received substantially less angiography (34.0%) and revascularization (11.4%) than Chinese (41.9%, 17.9%) and South Asians (40.0%, 16.3%). The ethnic disparity increased during the 1990s, particularly in the performance of coronary angiography (p = 0.038). While fatality declined during the study period for Chinese and South Asians, the rate remained stable for Malays. After a median follow-up period of 4.1 years, survival was lowest among Malays (adjusted HR, 1.28; 95% confidence interval, 1.15−1.42, compared with Chinese).

Conclusion: Ethnic inequalities in invasive cardiac procedures exist in Singapore and were exacerbated in the 1990s. Inequalities in medical care may contribute to the poorer long-term survival among Malays.

**Key words:** coronary angiography, coronary revascularization, ethnic, myocardial infarction, registry

#### Introduction

Ethnic differences in coronary mortality have been documented, and South Asians from the Indian subcontinent are particularly vulnerable. <sup>1,2</sup> While coronary mortality remained high among South Asians compared with Chinese or Malays in Singapore, we found that short- and long-term fatality following myocardial infarction (MI) was highest among Malays. <sup>3</sup> The reasons for this disparity remain unclear. One possible explanation may be related to variation in the utilization of invasive cardiac procedures following MI. There are significant differences in the use of invasive cardiac procedures following MI between black and white patients in the United States, <sup>4</sup> and between white and South Asians in the United Kingdom. <sup>5</sup> However, there is little information on the utiliza-

tion of revascularization procedures following MI in other ethnic groups and on possible inequalities in survival.

Singapore is a multiethnic society consisting of Chinese (77.0%), Malays (13.9%), and South Asians (7.7%), and it has a flourishing economy. Healthcare is easily accessible to all residents and is heavily subsidized by the government, including use of invasive cardiac procedures. This population provides an opportunity to explore ethnic differences, unimpeded by availability of services. Therefore, we assessed ethnic inequalities in the use of invasive cardiac procedures and considered the possible association between ethnic differences in long-term survival following MI.

#### **Materials and Methods**

The Singapore Myocardial Infarction Register<sup>6</sup> was established in 1987 to capture all MI events for all residents aged 20 to 64 years. Briefly, cases were identified from listings of all hospital discharges, creatine phosphokinase (CPK) from all biochemistry laboratories in Singapore, the National Death Registry, and postmortem reports. Trained investigators used modified World Health Organization multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) criteria<sup>7</sup> and Minnesota electrocardiographic coding.<sup>8</sup> To avoid a potential biasing effect of early mortality in an era when primary percutaneous transluminal coronary angioplasty (PTCA) for MI was rare, only those who survived 3 days were included in the analysis.

#### **Invasive Cardiac Procedures and Mortality**

In the Singapore healthcare financing system, residents have a compulsory saving scheme which may be withdrawn for medical treatment using the Central Claims Processing System. Deaths must be registered with the Registry of Births and Deaths ≤ 24 h. A unique identification number for each resident enabled linkage to these government databases to ascertain the type and date of invasive cardiac procedures and the date of death.

#### **Data Analysis**

Data management and analysis were performed using the Statistical Package for Social Sciences for Windows (SPSS, Inc., Chicago, Ill., USA). Internal checks were set up in the database to ensure the quality of the information.

Chi-square tests and analysis of variance or the Mann-Whitney U test were used to analyze differences in categorical and continuous variables, respectively. Kaplan-Meier estimates were obtained for long-term survival, and the log-rank test was used for comparison among groups. Multivariable analysis was performed using Cox proportional hazard modeling to determine ethnic associations with time to event, adjusting for covariates, namely, age, gender, typical symptoms, his-

tory of previous MI, peak CPK level, Q-wave MI, and use of coronary revascularization procedures ≤ 28 days. In analysis of ethnic associations with angiography, use of revascularization procedures was omitted from the model.

#### **Results**

From 1991 to 1999, 12,481 patients were classified as having MI, of whom 10,294 (82.5%) survived ≥ 3 days.

#### **Coronary Angiography**

During the study period, 4,175 (40.6%) patients underwent coronary angiography ( $\leq$  28 days after MI onset. Compared with those who did not undergo coronary angiography, they were younger (52 vs. 55 years; p<0.001), were less likely to be women (15.8 vs. 20.2%; p<0.001) and Malays (15.2 vs. 19.6%; p<0.001), and were less likely to have suffered from a previous MI (6.9 vs. 13.7%; p<0.001) or to have sustained a Q-wave MI (74.2 vs. 76.0%; p<0.001). They were more likely to present with typical symptoms (80.3 vs. 72.0%; p<0.001) and to have higher CPK levels (1,226 vs. 1,075 U/l; p<0.001). Crude rate of coronary angiography was lowest among Malays (Table I). After adjustment for baseline characteristics, Malays remained less likely to undergo coronary angiograpy (hazard ratio [HR] 0.82; 95% confidence interval [CI] 0.75–0.89; p<0.001) compared with Chinese.

#### **Coronary Revascularization**

Coronary revascularization  $\leq$  28 days after MI onset was performed in 16.5% of patients. Among patients who had coronary angiography, those undergoing revascularization were less likely to be Malays (12.3 vs. 17.1%; p<0.001) and to have suffered typical symptoms (78.2 vs. 81.8%; p=0.013) or a Q-wave MI (71.8 vs. 75.9; p=0.01). However, there was little difference with regard to age, peak CPK level, the proportion of women, and previous MI.

On multivariable adjustment, Malays were substantially less likely to undergo revascularization procedures than Chinese (HR 0.65; 95% CI, 0.56–0.75; p < 0.001), whereas rates between Chinese and South Asians were similar. Even among those who had coronary angiography, Malays remained less likely to receive revascularization (adjusted HR 0.79; 95% CI, 0.98–0.92; p = 0.002) compared with Chinese.

#### **Fatality**

The 1-year fatality was considerably lower among those who had angiography (5.0 vs. 18.8%; p < 0.001) and revascularization (4.5 vs. 14.3%; p < 0.001) than among those who had not. Among the three ethnic groups, the overall unadjusted 1-year mortality was highest among Malays (Table I). After a median 4.1-year (interquartile range 2.0–6.8) follow-up,

TABLE I Characteristics of patients of various ethnic groups with and without invasive cardiac procedures

	Chinese	Malay	South Asians	p Value
All patients				
Number	6,406	1,834	1,875	
Age, years <sup>a</sup>	55 (48, 60)	54 (46, 59)	53 (46, 60)	< 0.001
Male	5,215 (81.4)	1,482 (80.8)	1,550 (82.7)	0.41
Previous MI	598 (9.3)	233 (12.7)	275 (14.7)	< 0.001
Q-wave MI	4,797 (74.9)	1,399 (76.3)	1,407 (75.0)	0.36
Typical symptoms	4,773 (74.5)	1,373 (74.9)	1,467 (78.2)	0.001
Peak CPK level, IU/l a	1,160 (596, 2,498)	1,197 (651, 2,496)	1,009 (586, 2,083)	< 0.001
Angiography	2,715 (42.4)	633 (34.5)	757 (40.4)	< 0.001
Revascularization b	1,147 (17.9)	209 (11.4)	305 (16.3)	< 0.001
PTCA	883 (13.8)	149 (9.1)	235 (12.5)	< 0.001
CABG	302 (4.7)	68 (3.7)	75 (4.0)	0.14
1-year mortality	786 (12.3)	271 (14.8)	233 (12.4)	0.014
No coronary angiography				
Age, years <sup>a</sup>	56 (50,60)	55 (48,60)	55 (47,61)	< 0.001
Male	2,926 (79.3)	945 (78.7)	917 (82.0)	0.071
Previous MI	448 (12.1)	174 (14.5)	203 (18.2)	< 0.001
Q-wave MI	2,805 (76.0)	911 (75.9)	848 (75.8)	0.91
Typical symptoms	2,604 (70.5)	866 (72.1)	839 (75.0)	< 0.001
Peak CPK level, IU/l a	1,101 (588, 2,319)	1,146 (624, 2,350)	937 (561, 1,927)	0.001
1-year mortality	650 (17.6)	235 (19.6)	192 (17.2)	0.19
Angiograpy without revascularization				
Number	1,568	424	452	
Age, years <sup>a</sup>	52 (45, 59)	52 (44, 58)	41 (42, 57)	< 0.001
Male	1,347 (85.6)	357 (84.2)	379 (83.8)	0.072
Previous MI	82 (5.2)	37 (8.7)	45 (10.0)	0.007
Q-wave MI	1,176 (75.0)	331 (78.1)	345 (76.3)	0.64
Typical symptoms	1,281 (81.7)	340 (80.2)	378 (93.6)	0.79
Peak CPK level, IU/l a	1,236 (614, 2,820)	1,477 (685, 2,842)	1,084 (620, 2,241)	0.001
1-year mortality	85 (5.4)	28 (6.6)	25 (5.5)	0.76
Revascularization				
Age, years <sup>a</sup>	53 (47,59)	50 (44,56)	50 (45,59)	< 0.001
Male	942 (82.1)	180 (86.1)	254 (83.3)	0.32
Previous MI	68 (5.9)	22 (10.5)	27 (8.9)	0.012
Q-wave MI	816 (71.1)	157 (75.1)	214 (70.2)	0.17
Typical symptoms	888 (77.4)	167 (79.9)	250 (82.0)	0.22
Peak CPK level, IU/l a	1,240 (596, 2,782)	1,208 (687, 2,715)	1,201 (628, 2,657)	0.88
1-year mortality	51 (4.4)	8 (3.8)	16 (5.2)	0.80

<sup>179</sup> patients were from other ethnic groups.

Abbreviations: MI = myocardial infarction, CPK = creatine phosphokinase, PTCA = percutaneous transluminal coronary angioplasty, CABG = coronary artery bypass graft.

mortality remained higher among Malays (adjusted HR 1.28; 95% CI, 1.15-1.42; p<0.0001, vs. Chinese).

Long-term fatality was lower among patients undergoing coronary angiography (adjusted HR 0.47; 95% CI, 0.42–0.53; p<0.0001). Compared with patients not receiving revascularization, those who did had better long-term survival (adjusted HR 0.41; 95% CI, 0.37–0.45), which was uniformly true across all three ethnic groups (p = 0.8) (Fig. 1A). The excess in long-term mortality among Malays was restricted to

those who did not undergo revascularization  $\leq$  28 days (p < 0.0001) (Fig. 1B).

## $\label{thm:condition} \begin{tabular}{l} Trends in Utilization of Invasive Cardiac Procedures \\ and Fatality (Table II) \end{tabular}$

To evaluate the rates of diffusion of invasive cardiac procedures, we divided the study into two periods: 1991–1995 and

Values are expressed as numbers with percentages in parentheses.

<sup>&</sup>lt;sup>a</sup> Median and interquartile range.

<sup>&</sup>lt;sup>b</sup> Some patients received two revascularization procedures.

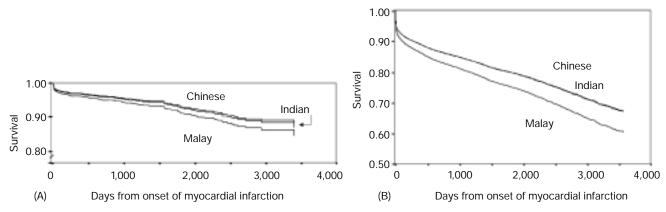


Fig. 1 Long-term survival among patients with (A) and without (B) coronary revascularization following myocardial infarction among the three ethnic groups.

1996–1999. While Malays were less likely to receive coronary angiography than non-Malays in the first period (p = 0.047), the difference increased substantially in the second period (p < 0.001). Malays were less likely to undergo revascularization procedures, particularly PTCA (p < 0.001), in both periods. The increased ethnic disparity in invasive procedures was modeled by interaction terms of ethnicity and period, which was statistically significant for the use of coronary angiography (p = 0.038) but not for revascularization procedures. Among those who had coronary angiography, the adjusted HR for Malays to receive coronary revascularization procedures was 0.76 (95% CI, 0.56–0.98; p = 0.036) and 0.80 (95% CI, 0.66–0.96; p = 0.019) in the first and second time periods, respectively.

Crude 1-year fatality declined considerably over the two time periods for Chinese and South Asians, without similar change for Malays. However, an interaction term between ethnicity and period was not significant in a Cox regression model adjusted for age and gender.

#### Discussion

Malays in Singapore were less likely to undergo coronary angiography and revascularization procedures ≤ 28 days, and short- and long-term mortality was higher than that in Chinese or South Asians, even after adjusting for baseline characteristics. However, the striking mortality difference between those who did and did not undergo coronary angiography appears to be overwhelmingly attributable to patient selection. Our study population was limited to 3-day survivors of MI, thus excluding patients who died early without an opportunity for invasive cardiac procedures. Indeed, patients who underwent coronary angiography without revascularization had lower mortality than those who did not have invasive procedures. Notably, we found significant growth in the utilization of coronary angiography in the period from 1991–1995 to 1996– 1999 among Chinese and South Asians, but not Malays. While the rates of coronary revascularization procedures rose

TABLE II Use of invasive cardiac procedures in patients with myocardial infarction of various ethnic groups during the two time periods

	Chinese		Malay		South Asians		Total		
Period No. of patients	1991–1995 3,323	1996–1999 3,083	1991–1995 921	1996–1999 913	1991–1995 1,031	1996–1999 844	1991–1995 5,399	1996–1999 4,895	p Value interaction <sup>e</sup>
Coronary									
angiography	1,299 (39.1)	1,416 (45.9) a	315 (34.2)	318 (34.8)	353 (34.2)	404 (47.9) a	2,011 (37.2)	2,162 (7.3) a	0.038
Revascularization	408 (12.3)	739 (24.0) a	76 (8.3)	133 (14.6) a	104 (10.1)	201 (23.8) a	609 (11.3)	1,092 (22.3)	0.45
PTCA	264 (7.9)	909 (18.6) a	40 (4.3)	109 (11.9) a	70 (6.8)	165 (19.5) a	388 (7.2)	909 (18.6) a	0.68
CABG	160 (4.8)	142 (4.6)	39 (4.2)	29 (3.2)	36 (3.5)	39 (4.6)	242 (4.5)	214 (4.4)	0.30
1-year fatality	439 (13.2)	347 (11.3) b	137 (14.9)	134 (14.7)	146 (14.2)	87 (10.3) <sup>c</sup>	731 (13.5)	575 (11.7) <sup>d</sup>	0.13

P values are for comparison between two time periods within each ethnic group.

<sup>&</sup>lt;sup>a</sup> p<0.001.

 $<sup>^{</sup>b}$  p = 0.017.

 $<sup>^{</sup>c}$  p = 0.012.

 $<sup>^{</sup>d}$  p = 0.006.

<sup>&</sup>lt;sup>e</sup> P value for interaction term (product between ethnicity [1 = Malay, 0 = non-Malay] and period [0,1]) in logistic model adjusted for age and gender. Abbreviations as in Table I.

for all three ethnic groups over the same period, Malays had the smallest absolute and relative increase. In fact, Malays who had undergone angiography were less likely to undergo revascularization procedures in both time periods. A disturbing observation was the lack of decline in fatality among Malays over the study period, in contrast to a substantial fall among Chinese and South Asians. Other than chance (a formal test for a differential decline was not statistically significant), possible explanations for the raised mortality in Malays may relate to inequalities of medical care, including lower rates of revascularization, and other factors, such as characteristics of the MI or response to therapy.

Favorable effects of routine revascularization following MI also remain uncertain. Elective reopening of an occluded vessel may prevent remodeling of the left ventricle after an anterior wall MI and may reduce subsequent adverse events. While left ventricular volumes have been reported to decrease and increase following late reperfusion of MI, there was a corresponding reduction in adverse cardiovascular events, following late reperfusion of the second in the second in adverse cardiovascular events, following late reperfusion of the second in the second in

Reports on ethnic differences in coronary interventions and fatality have largely been confined to the United States population. Several studies have shown that black patients were less likely to undergo coronary angiography, <sup>12</sup> PTCA, and coronary artery bypass surgery (CABG).<sup>12, 13</sup> Even among patients who underwent coronary angiography, the patterns of subsequent revascularization differ between blacks and whites; 14 blacks were less likely to receive revascularization. Other ethnic groups, including Hispanics and Asian Americans, were also less likely to undergo invasive cardiac procedures in the United States, 15 which may be "overused" among whites. 16 Among patients in whom revascularization was considered appropriate, South Asians were less likely to undergo the procedure, particularly CABG, than whites in the United Kingdom.<sup>5</sup> However, there was no difference in mortality and nonfatal MI, in contrast to our findings. We cannot directly attribute the excess fatality in Malays to their lower rates of revascularization because of strong forces of selection and the persistence of ethnic differences after adjustment for revascularization.

A patient's socioeconomic status, clinical characteristics, and knowledge of cardiac risk factors may relate to preference for invasive cardiac procedures.<sup>17</sup> Those with less than high school education, current smokers, and blacks<sup>18</sup> were more likely to dismiss a recommendation for coronary angiography. Other factors, such as trust in the medical system and adversity to invasive procedures, may also contribute to these variations. 19 Cultural and social factors relating to understanding of disease and treatment play a critical role in determining ethnic differences in invasive procedures. Malays, who on average are less educated than Chinese or South Asians, were less likely to undergo angiography and revascularization. Even among those who had angiography, Malays had significantly less revascularization procedures, which may be attributed to variations in atherosclerotic lesion patterns, differences in acceptance of recommendations of revascularization, and physician behavior.

The higher fatality among Malays could not be readily explained by adverse available clinical characteristics. Although peak CPK levels were highest among Malay patients, suggesting larger infarctions, the absolute variations were small and unlikely to be clinically significant, <sup>20</sup> and differences persisted after statistical adjustment. Information on heart failure was not available.

While our Registry included all Singapore residents throughout the 1990s, only those aged < 65 years were studied. A substantial proportion (~40%) of patients with MI was excluded. We did not collect data on acute and chronic medical care; therefore, we do not know whether the use of evidence-based efficacious drugs might explain ethnic differences in survival. From 2000, our Registry has expanded to include residents of all ages and clinical comorbidities, drug utilization, and procedures.

#### Conclusion

Malay patients were less likely to undergo coronary angiography and revascularization procedures, and they had a poorer prognosis. The determinants of these differences remain to be clarified. Inequalities in medical care may contribute to the mortality differential.

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### Images in Cardiology: Heterotopic Heart Transplantation

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Fig. 1 Electrocardiogram revealing atrial fibrillation in the recipient's heart and normal rhythm in the donor's heart, which was totally paced via a permanent pacemaker with corresponding distal aortic (AO) pressure (scale 0–150 mmHg).

A 64-year-old man who had undergone heterotopic heart transplantation (HHT) in 1993 was admitted to our hospital because of shortness of breath. The patient developed multiorgan failure due to gram negative urosepsis and succumbed on the 27th day (Figs.1, 2).

Barnard and Losman first carried out a form of HHT in 1974, whereby the donor heart acted as a left ventricular assist device. Yacoub and co-workers subsequently performed it successfully in a number of patients. Heterotopic heart transplantation is indicated in patients with severe, nonreversible



Fig. 2 Echocardiogram demonstrating donor's (d) and recipient's (r) hearts. LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle, Ao = Aorta

pulmonary hypertension and in cases of a large discrepancy in body mass (>33%) between the donor and the recipient.

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