



Clinical outcomes of elderly South-East Asian patients in primary percutaneous coronary intervention for ST-elevation myocardial infarction

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Abstract

Objective To evaluate the clinical characteristics and in-hospital outcomes of elderly South-East Asian patients undergoing primary percutaneous coronary intervention (PPCI). **Methods** From January 2009 to December 2012, 1268 patients (86.4% male, mean age of 58.4 ± 12.2 years) presented to our hospital for ST-elevation myocardial infarction (STEMI) and underwent PPCI. They were divided into two groups: elderly group defined as age ≥ 70 years and non-elderly group defined as age < 70 years. Data were collected retrospectively on baseline clinical characteristics, door-to-balloon (D2B) time, angiographic findings, therapeutic modality and hospital course. **Results** The elderly group constituted 19% of the study population with mean age 76.6 ± 5.0 years. There was a higher proportion of female gender and ethnic Chinese patients in the elderly group when compared with the non-elderly group. The former was less likely to be smokers and have a significantly higher prevalence of hypertension. The mean D2B time was significantly longer in the elderly group. They also had a significantly higher incidence of triple vessel disease and obstructive left main disease. The use of radial artery access, glycoprotein 2b/3a inhibitors and drug-eluting stents during PPCI were also significantly lower. In-hospital mortality was significantly higher in the elderly group. The rate of cardiogenic shock and in-hospital complications were also significantly higher. **Conclusions** Our registry showed that in-hospital mortality rate in elderly South-East Asian patients undergoing PPCI for STEMI was high. Further studies into the optimal STEMI management strategy for these elderly patients are warranted.

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1 Introduction

Cardiovascular disease is a growing health burden across Asia and this is fuelled by increasing rates of diabetes mellitus, hyperlipidemia, hypertension, obesity and unhealthy life-style choices in the region.^[1,2] Several countries in Asia including Singapore are also facing the silver tsunami which is associated with increased risk of cardiovascular complications.^[3,4] The local population in Singapore is ageing rapidly as the number of persons aged ≥ 65 years will escalate from 9% in 2008 to approximately 19% of local population in 2030. The prevalence of cardiovascular disease is expected to rise and as a result, will pose a significant challenge and burden to the local health system.

Previous cardiovascular studies have shown that elderly patients were less likely to receive evidence-based therapies and had higher mortality rate.^[5–8] There was also marked variation in the clinical care of the elderly with acute coronary syndromes (ACS).^[5–7] In addition, limited data are available on the delivery of health care and clinical outcomes of elderly patients with cardiovascular disease in the South-East Asia region. We therefore sought to evaluate the clinical characteristics and in-hospital outcomes of our cohort of elderly South-East Asian patients undergoing primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) in “real world” clinical practice.

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2 Methods

2.1 Study population and design

From January 2009 to December 2012, a total of 1268 consecutive patients were diagnosed with STEMI and un-

derwent PPCI at our institution, a tertiary referral centre in Singapore. Data were collected retrospectively on baseline clinical characteristics, presenting signs and symptoms, door-to-balloon (D2B) time, angiographic findings, therapeutic modality and hospital course.

2.2 Interventional procedure

All PCIs were performed using standard techniques and according to current practice guidelines. All patients were treated with aspirin (an oral loading dose of 300 mg followed by 100 mg daily) prior to the procedure and indefinitely thereafter. Patients also received clopidogrel (an oral loading dose of 300 mg followed by 75 mg daily) before the procedure, followed by a minimum of four weeks in patients who received bare metal stent (BMS) and one year in patients who received drug-eluting stent (DES). Additional duration of clopidogrel treatment was at the discretion of the attending physician.

2.3 Definitions and outcomes

In our study, we defined elderly as those with age ≥ 70 years and those aged < 70 years formed the comparison group. Myocardial infarction (MI) was defined according to the latest consensus on MI definition,^[9] along with the presence of typical symptoms, and/or electrocardiographic changes suggestive of infarction or ischaemia that was associated with a rise of cardiac troponins to at least twice the upper limit of the normal value. The culprit lesion for STEMI was identified based on morphology including complete occlusion, thrombus and ulcerative stenosis or assumed to be the tightest stenosis if these features were absent. Angiographic stenosis was defined as diameter reduction of $\geq 50\%$. PCI procedural success was defined as successful restoration of thrombolysis in myocardial infarction (TIMI) 3 flow after stenting or balloon angioplasty. The major clinical outcomes (in-hospital) analysed in our study include all-cause mortality, Killip III-IV, major arrhythmia events (complete heart block, atrial, and ventricular arrhythmias), cerebrovascular accident (CVA), sepsis and cardiogenic shock. Bleeding complications were defined according to TIMI bleeding criteria.

2.4 Statistical analysis

Continuous variables were expressed as mean \pm SD. Dichotomous variables were expressed as *n* (%). Statistical comparisons were performed using the Student *t* test, Chi square test, or Fisher's exact test, as appropriate. Calculations were performed using SPSS software (version 16.0). Two sided significance level of 0.05 was chosen for all the

tests. All investigations were carried out in accordance with the Declaration of Helsinki and the study was approved by the local ethics committee.

3 Results

Table 1 summarizes the baseline clinical characteristics of the study population. For the overall study group, the mean age at presentation was 58.4 ± 12.2 years, with male predominance (86.4%). The elderly group constituted 19.4% of the study population with mean age 76.6 ± 5.2 years.

When compared to their younger counterparts, the elderly group more likely to be female, of Chinese ethnicity, and have a higher rate of hypertension. The former group, however, were more likely to be smokers. No significant differences were observed for both groups with respect to cardiovascular risk factors, such as diabetes mellitus, hyperlipidaemia, prior MI, prior PCI or prior coronary artery bypass grafting (CABG) and end-stage renal failure on dialysis. Types of STEMI presentation also did not differ in

Table 1. Baseline clinical characteristics.

	Overall (<i>n</i> = 1268)	Elderly (<i>n</i> = 245)	Non-elderly (<i>n</i> = 1023)	<i>P</i>
Age, yrs	58.4 \pm 12.2	76.6 \pm 5.2	54.0 \pm 8.9	< 0.001
Male/Female	1096/172	170/75	926/97	< 0.001
Ethnicity				
Malay	184 (14.5%)	21 (8.6%)	163 (15.9%)	
Chinese	819 (64.6%)	194 (79.2%)	625 (61.1%)	< 0.001
Indian	202 (15.9%)	25 (10.2%)	177 (17.3%)	
Others	63 (5%)	5 (2.0%)	58 (5.7%)	
Ever smoker	671 (53%)	90 (37%)	581 (57%)	< 0.001
Diabetes mellitus	365 (28.8%)	76 (31%)	289 (28.3%)	0.4
Hypertension	664 (52.4%)	159 (64.9%)	505 (49.4%)	< 0.001
Hyperlipidemia	680 (53.6%)	142 (58.0%)	538 (52.6%)	0.13
Prior MI	129 (10.2%)	32 (13.1%)	97 (9.5%)	0.09
Prior PCI	103 (8.1%)	19 (7.8%)	84 (8.2%)	0.83
Prior CABG	6 (0.5%)	2 (0.8%)	4 (0.4%)	0.38
Renal failure on dialysis	11 (0.9%)	3 (1.2%)	8 (0.8%)	0.45
Type of AMI				
Anterior	595 (47%)	105 (42.9%)	490 (48%)	
Inferior	599 (47.4%)	127 (51.8%)	472 (46.3%)	
Posterior	19 (1.5%)	4 (1.6%)	15 (1.5%)	0.45
Others	52 (4.1%)	9 (3.7%)	43 (4.2%)	
LVEF, %	41 \pm 11	39 \pm 12	41 \pm 11	0.002
Self-present/EMS	495/772	90/155	405/617	0.4

Data were expressed as mean \pm SD, *n* (%) or *n*. AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; EMS: emergency medical services; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention.

both groups but the mean left ventricular function was significantly lower in the elderly group. As for mode of presentation to hospital, both groups (> 60%) were equally likely to use emergency medical services (EMS) rather than self-present to hospital.

Table 2 summarizes the D2B time, angiographic findings and procedural variables of the study population. For the overall study group, the mean D2B time was 68 ± 35 min. The mean symptom onset to reperfusion time was 256 ± 224 min. The elderly group had a significantly longer mean D2B time when compared to the non-elderly group. The mean symptom onset to reperfusion time was numerically higher in the elderly group but was not statistically significant.

The former group had a higher proportion of triple vessel disease and occlusive left main disease on coronary angiography. The most common target vessel for PCI for the elderly group was right coronary artery (RCA) whereas it was the left anterior descending artery (LAD) for the non-elderly group. Femoral access (> 70%) was used more frequently than radial access in the elderly group when compared to the non-elderly group. Usage of glycoprotein IIb/IIIa inhibitors was also significantly lower in the former group. The majority of patients (> 80%) in both groups underwent stenting during PPCI but the elderly group were less likely to receive a DES implantation. Pure old balloon angioplasty (POBA) was also used more frequently in the elderly group.

Table 3 summarizes the clinical outcomes (in-hospital) of the study population. The overall in-hospital mortality for the study group was 5.2%. The elderly group had a significantly higher in-hospital mortality (11.9% *vs.* 3.6%) when compared to their younger counterparts. They were much sicker at presentation (higher proportion of Killip III-IV) and had a higher rate of cardiogenic shock thus requiring a higher use of IABP.

No difference was observed between both groups in terms of developing life-threatening ventricular arrhythmias. However, the elderly group were more likely to develop atrial arrhythmias (atrial fibrillation/flutter) and complete heart block. The rates of CVA (ischaemic/hemorrhagic) were similar for both groups. Sepsis also occurred more frequently in the elderly group. The most common cause of sepsis in both groups was pneumonia followed by urinary tract infection.

The overall bleeding rate for the study group was 10.2%. There were increased bleeding episodes (18.8% *vs.* 8.1%) in the elderly group patients when compared to their younger counterparts. Significant bleeding (TIMI I-II) also occurred at a higher rate in the elderly group compared to the younger population (13.9% *vs.* 3.7%). The mean length of hospital stay was similar in both groups.

4 Discussion

As Asia braces for an unprecedented “silver tsunami”,

Table 2. D2B time, angiographic findings and procedural variables of patients.

	Overall (n = 1268)	Elderly (n = 245)	Non-Elderly (n = 1023)	P
Mean D2B, min	68 ± 35	74 ± 35	66 ± 34	0.003
Symptom onset to reperfusion, min	256 ± 224	270 ± 212	253 ± 226	0.34
Number of diseased vessels on angiography				
1	412 (32.5%)	48 (19.7%)	364 (35.7%)	0.001
2	416 (32.8%)	77 (31.6%)	339 (33.2%)	0.62
3	437 (34.5%)	119 (48.8%)	318 (31.1%)	0.001
Target vessel				
LAD	605 (47.7%)	102 (41.6%)	503 (49.2%)	0.03
RCA	501 (39.5%)	116 (47.3%)	385 (37.6%)	0.005
CIRC	115 (9.1%)	13 (5.3%)	102 (10%)	0.02
Left main	37 (2.9%)	12 (4.9%)	25 (2.4%)	0.04
Others	10 (0.8%)	2 (0.8%)	8 (0.8%)	0.96
Femoral/radial access	800/461	179/65	621/396	0.001
GpIIb/IIIa	921 (72.6%)	158 (64.5%)	763 (74.6%)	0.002
POBA/Stent	158/1110	42/203	116/907	0.01
BMS/DES	655/455	152/51	503/404	0.001

Data were expressed as mean ± SD, n (%) or n. BMS: bare metal stent; CIRC: left circumflex; DES: drug-eluting stent; D2B: door-to-balloon; IABP: intra-aortic balloon pump; GpIIb/IIIa: glycoprotein IIb/IIIa inhibitors; LAD: left anterior descending artery; POBA: pure old balloon angioplasty; RCA: right coronary artery.

Table 3. In-hospital clinical outcomes.

Inpatient complications	Overall (n = 1268)	Elderly (n = 245)	Non-elderly (n = 1023)	P
In-hospital mortality	66 (5.2%)	29 (11.9%)	37 (3.6%)	0.001
PCI procedural (for those who died)				
Success		24 (83%)	31 (84%)	1.00
Failure		5 (17%)	6 (16%)	
Killip class III/IV	265 (20.9%)	71 (29.0%)	194 (19.0%)	0.001
Cardiogenic shock	258 (20.5%)	61 (25.2%)	197 (19.4%)	0.04
IABP	167 (13.2%)	44 (18%)	123 (12%)	0.01
CVA (haemorrhagic, ischemic)	11 (0.9%)	2 (0.8%)	9 (0.9%)	0.92
VT/VF	158 (12.5%)	34 (13.9%)	124 (12.1%)	0.45
AF/Flutter	86 (6.8%)	33 (13.5%)	53 (5.2%)	0.001
Heart block	84 (6.6%)	24 (9.8%)	60 (5.9%)	0.03
Sepsis	136 (10.7%)	48 (19.6%)	88 (8.6%)	0.001
Pneumonia	90 (66.1%)	33 (68.8%)	57 (64.8%)	0.707
UTI	13 (9.6%)	5 (10.4%)	8 (9.1%)	0.770
Others	8 (5.9%)	2 (4.2%)	6 (6.8%)	0.712
Unknown	25 (18.4%)	8 (16.7%)	17 (19.3%)	0.818
Any TIMI bleeding	129 (10.2%)	46 (18.8%)	83 (8.1%)	0.001
TIMI bleeding I-II	72 (5.7%)	34 (13.9%)	38 (3.7%)	0.003
Mean length of hospital stay, day	6 ± 9	7 ± 7	6 ± 10	0.1

Data were expressed as mean ± SD, n (%). AF: atrial fibrillation; CVA: cerebrovascular accident; IABP: intra-aortic balloon pump; PCI: percutaneous coronary intervention; TIMI: thrombolysis in myocardial infarction; UTI: urinary tract infection; VF: ventricular fibrillation; VT: ventricular tachycardia.

increasing numbers of elderly patients are seeking medical care for ACS or symptoms of cardiovascular disease.^[3,4] The clinical outcomes of elderly patients who undergo PCI especially for Asian patients remains under-represented in the published literature.^[10-12] Elderly patients represented 19.4% of our study population and to our knowledge, this is the first observational study reporting the clinical outcomes of elderly STEMI patients undergoing PPCI in real world clinical practice in the South-East Asian region.

The elderly group in our study more likely to be female, have a higher rate of hypertension but were less likely to be smokers. This is partially consistent with the findings of other studies that have shown elderly patients are often female, have higher rate of hypertension, diabetes mellitus, prior MI and prior CABG.^[5,7]

There are more Chinese in the elderly group of patients in Singapore which is likely a reflection of the local ethnic composition. Singapore is a South-East Asian city-state which has a multiethnic population of 5.5 million. Based on the government census report, the ethnic compositions of Malays, Chinese and Indians in the general population were 13.4%, 74.2% and 9.2%, respectively.

The elderly group in our study had a significantly longer mean D2B time when compared to non-elderly group although the symptom onset to reperfusion time was similar in both groups. A major reason for the delay in D2B as re-

ported by prior studies is due to the atypical presentation of ACS in the elderly which is often non-specific.^[13,14] Dyspnoea is the more common presenting complaint compared to precordial chest pain and they could also present with epigastric discomfort, giddiness or delirium. Barriers to effective communication and proper consent taking such as impaired hearing function, vision and cognitive function, could also potentially prolong D2B time. In Asia, family members customarily play an important role in the care of the patient. Hence, informed consent for procedures is commonly shared between various family members and the patient. These factors may lead to delay in consent-taking, thus resulting in delay in medical intervention.

The elderly group also had a higher proportion of triple vessel disease and occlusive left main disease on coronary angiography when compared to their younger counterparts. This finding is consistent with prior studies and is likely a clinical manifestation of the natural history of coronary atherosclerosis, i.e., an age-dependent chronic inflammatory process.^[15-18]

In our study, femoral access (> 70%) was used more frequently as a default route than radial access in the elderly group when compared to the non-elderly group. This is likely due to selection bias as the elderly patients tend to have weaker radial pulses because of advanced atherosclerosis and much sicker at presentation, thus precluding

radial access. Age should not be a barrier to transradial access for PCI if feasible as studies have shown better clinical outcomes with transradial approach compared to transfemoral approach.^[19–21]

The majority of patients (> 80%) in both groups underwent stenting during PPCI but the elderly group was less likely to receive a DES implantation. Pure old balloon angioplasty was used more frequently in the elderly group and usage of glycoprotein IIb/IIIa inhibitors was also significantly lower. This could be explained by concerns of increased bleeding risks in the elderly and their inability to tolerate prolonged dual anti-platelet therapy (DAPT). There have been several studies which have reported advanced age as a predictor of bleeding and mortality.^[22,23] The overall bleeding rate for the study group was 10.2%. There were increased bleeding episodes in the elderly group patients when compared to their younger counterparts (18.8% vs. 8.1%). Significant bleeding (TIMI Bleeding I-II) also occurred at a higher rate in the elderly group compared to the younger population (13.9% vs. 3.7%). The elderly group of patients may potentially benefit from the advent of newer generation DES especially polymer-free DES which is safe with a shorter duration of DAPT and associated with better outcomes when compared to BMS.^[24]

Prior studies have shown that age-dependent inequalities are apparent in the management of ACS with elderly patients less likely to undergo cardiac catheterisation and PCI.^[5–7] In Singapore, PPCI is the default reperfusion therapy for patients with STEMI and there's no age limit even for elderly patients (oldest patient in our study was 94 years old). Despite getting full access to PPCI, the mortality rate is quite high (11.9%) in our cohort of elderly patients when compared to their younger counterparts. This is consistent with the findings of previous studies that had demonstrated that increased age was associated with higher in-hospital morbidity and mortality.^[25–27] By multivariate analysis, elderly group was an independent predictor of in-hospital mortality in our study with an odds ratio of 3.1 (95% confidence interval: 1.7–5.6; $P = 0.001$).

Aging inevitably causes a number of physiological and morphological changes in the body that can alter cardiovascular function. As a result of multiple co-morbidities, elderly patients have lower cardiac reserve and lower capacity to recover from acute cardiac injury than their younger counterparts. The elderly group in our study was much sicker at presentation (higher proportion of Killip Class III-IV), had more extensive coronary artery disease, a longer D2B time and received lower use of contemporary pharmacoinvasive treatment during PPCI. They were also more

prone to develop major in-hospital complications like tachybradyarrhythmias, sepsis and bleeding complications when compared to the younger group. PCI procedural failure is associated with advanced age but this was not observed as a contributory factor for higher rate of in-hospital mortality in our study (Table 3).

4.1 Study limitations

There were several limitations to our study. Our sample size was relatively small when compared to other studies. Moreover, our study was a retrospective, single-centre observational study. Thus, selection bias was inevitable and would impact on our findings. We also did not capture data on the prevalence of antecedent risk factors like atrial fibrillation, previous CVA, peripheral vascular disease and chronic obstructive lung disease which may impact clinical outcomes especially in the elderly group.

4.2 Conclusions

Despite having an advanced medical health system in Singapore, our registry showed that the in-hospital mortality rate in elderly South-East Asian patients undergoing PPCI for STEMI was high. They had more extensive coronary artery disease, a longer D2B time and lower use of contemporary pharmacoinvasive treatment during PPCI which could account for their poorer prognosis. Further studies into the optimal STEMI management strategy for the elderly patients are warranted.

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