Comparing Clinical Outcomes between Elderly and Younger Patients Receiving Primary Percutaneous Coronary Intervention

Lu-Yu Ying, Ming-Jer Hsieh, Chun-Chi Chen, Chao-Yung Wang, Shang-Hung Chang, Cheng-Hung Lee, Dong-Yi Chen, Ming-Lung Tsai, Ming-Yun Ho, Jih-Kai Yeh, Yu-Chang Huang, I-Chang Hsieh

Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, , Taoyuan, Taiwan

Abstract

Background: In this study, we aimed to elucidate age-related clinical characteristics and outcome differences in patients receiving primary percutaneous coronary intervention (PPCI) in Taiwan.

Methods and results: A total of 967 patients with acute myocardial infarction who underwent PPCI between April 2005 and August 2016 were enrolled in this study. The patients were categorized into four age groups: Quartile 1, 25-50 yrs old (24.8%); Quartile 2, 51-59 yrs (25.1%); Quartile 3, 60-69 yrs (25%); and Quartile 4, ≥ 70 yrs old (25%). After 4 years of follow-up, the oldest age group (age ≥ 70 yrs) had double the crude risk of total major adverse cardiovascular events (MACE), compared to the youngest age group (age 25-50 yrs) (hazard ratio (HR): 2.04, 95% confidence interval (CI): 1.35-3.07, adjusted p=0.001), which was mainly driven by all-cause mortality (HR: 3.83, 95% CI: 1.56-9.37, p=0.003). However, after adjusting for underlying comorbidities, age was not an independent predictor of MACE (HR: 1.42, 95% CI: 0.93-2.18, p=0.109). There was no statistically significant difference in recurrent myocardial infarction, repeat revascularization or in-hospital mortality between the older and younger groups.

Conclusions: In our study, older patients had higher all-cause mortality in the setting of PPCI without significant differences in in-hospital mortality, recurrent myocardial infarction and repeat revascularization, compared with their younger counterparts. This suggested that prompt revascularization and other constitutional and modifiable risk factors are equally important in PPCI, as MACE is not due to age alone.

Keywords: acute myocardial infarction, elderly patients, age, primary PCI

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Address for correspondence: I-Chang Hsieh, MD
Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital, Chang Gung University College of Medicine; No. 5, Fu-Hsing Street, Kwei-Shan, Taoyuan, Taiwan
E-mail: hsiehic@ms28.hinet.net

Introduction

Primary percutaneous coronary intervention (PPCI) is the dominant reperfusion strategy in Taiwan owing to the convenience of medical access and medical insurance in the country.[1] Both young and elderly patients are usually under-represented in major randomized controlled trials involving PPCI.[2,3] Presumably, practitioners consider the risk-benefit ratio of cardiac procedures to be less favorable in the elderly, possibly due to their frailty, lower life expectancy, and higher risk of bleeding or kidney injury, etc.[4,5] Several studies have evaluated age-related outcome differences in these populations, some focusing on elderly patients,[4-19] and others focusing on the young.[20,21] Studies evaluating age-related differences in outcomes after PPCI found that elderly patients have a worse prognosis than young patients.[4-9,11] However, in these studies, PPCI was not the first-line management choice.[16,18] Another study showed that mortality reduction by PPCI was independent of the patient's age.[22] In real-world practice, elderly patients are less likely to receive standard and timely coronary reperfusion therapy than younger patients.[6,23] It remains unknown whether outcome differences between these groups are age-related. This study aimed to compare the outcomes of PPCI among different age quartiles in a tertiary medical institute in Taiwan.

Methods

Study data and patient source

A total of 967 patients with acute myocardial infarction (MI) who underwent PPCI between April 2005 and August 2016 were identified in the Cardiovascular Atherosclerosis and Percutaneous Transluminal Interventions (CAPTAIN) registry, a prospective, physician-initiated, single-center observational database maintained in Taiwan since November 1995. This is an ongoing registry that includes the data of 8,100 consecutive patients who successfully underwent elective and primary percutaneous coronary intervention (PCI) with stenting from November 1995 to August 2020. Patients were equally divided into four groups according to age: Quartile 1 (Q1): 25-50 years old; Quartile 2 (Q2): 51-59 years; Quartile 3 (Q3): 60-69 years; Quartile 4 (Q4): ≥ 70 years old. All patients were followed up for 4 years. The outcomes of interest were recurrent myocardial infarction, any revascularization (target lesion revascularization or new lesion requiring stenting), in-hospital mortality, all-cause mortality, and major adverse cardiovascular events (MACEs) (defined as a composite of myocardial infarction, revascularization, and all-cause mortality after index PCI, during the 4 years). The date of the outcome was verified based on medical records or phone contact. Ethical approval for this study was obtained from the institutional review board of the Chang Gung Medical Foundation. All patients provided informed consent to undergo PCI and the follow-up protocol, in addition to providing consent to publish the case details.

Statistical analysis

SPSS23 (IBM, USA) statistical software was used for all statistical analyses. The basic characteristics were compared using either analysis of variance or the chi-squared test, and reported as mean ± standard deviation (SD) or percentage for continuous and categorical variables, respectively. Kaplan-Meier analysis was used to assess the associations between the four quartiles and total MACEs. Survival curves were compared using the log-rank test. Cox proportional hazard regression analysis was used to assess univariate and multivariate associations of age groups with mortality, adjusting for potential confounders including sex, hypertension, diabetes mellitus, hyperlipidemia, smoking, family history of coronary artery disease, previous stroke, left ventricular ejection fraction (LVEF) < 40%, multivessel disease (defined as ≥50% diameter stenosis in at least two major epicardial coronary vessels or their major branches), calcified lesion, Killip class 3 or 4, chronic kidney disease (CKD), ST-segment elevation myocardial infarction

(STEMI), culprit lesion in the left anterior descending artery (LAD), use of drug-eluting stent (DES) or not and onset-to-reperfusion time > 12 hours. Statistical significance was set at $P < 0.05$.

Result

A total of 967 patients were enrolled in this study. They were equally divided into four different age groups: Q1: age: 25-50 years, 240 patients; Q2: age: 51-59 years, 243 patients; Q3: age: 60-69 years, 242 patients; and Q4: age: ≥ 70 years, 242 patients. Table 1 shows the clinical characteristics of the 4 different age groups. Significant trends in older patients included a higher prevalence of female patients, comorbidities including hypertension, diabetes mellitus, previous stroke, chronic kidney disease, and disease complexity (probability of depressed LVEF, multi-vessel disease, Killip class, and calcified lesion), and higher high-sensitivity C-reactive protein (hs-CRP) levels. By contrast, among young patients there was more smoking, hyperlipidemia, and higher levels of creatinine kinase MB (CK-MB), low-density lipoprotein cholesterol, and total cholesterol at presentation. Younger patients more frequently presented with LAD as the culprit vessel. The percentage of DES use was similar across all the groups. Although older patients had more multi-vessel disease, they were less likely to receive complete revascularization than others. Table 2 shows the follow-up outcomes, by years, of patients post PPCI, according to age quartile. Ascending cross the four age-groups, the oldest age groups had higher unadjusted all-cause mortality (2.5% vs. 4.1% vs. 6.2% vs. 19%, p<0.001), in-hospital mortality (2.1% vs. 2.5% vs. 2.5% vs. 7.4%, p= 0.009), and MACEs (14.6% vs. 16.5% vs. 21.1% vs. 26.9%, p=0.001). However, differences in current MI (2.5% vs. 2.1% vs. 5.0% vs. 4.1%, p=0.156) or any revascularization (11.7% vs. 11.9% vs. 14.9% vs. 8.7%, p=0.259) were not statistically significant between the groups. After adjusting for clinical variables, the oldest age group had comparable rates of recurrent MI (p=0.190), any revascularization (p=0.208), in-hospital mortality, and MACE (p=0.599), compared to the other groups. Table 3 shows the predictors of MACE in multivariate analysis. Female sex (adjusted hazard ratio (HR): 1.49, 95% confidence interval (CI): 1.05-2.12, p=0.025), history of stroke (adjusted HR: 2.29; 95% CI: 1.41-3.74], p=0.001), CKD (adjusted HR: 2.98; 95% CI: 1.92-4.64; p<0.001), and multi-vessel disease (adjusted HR: 1.52; 95% CI: 1.01-2.29, p=0.045) were associated with higher MACE. The use of DES (adjusted HR: 0.68; 95% CI: 0.51-0.90; p=0.008) and complete revascularization (adjusted HR: 0.63; 95% CI: 0.43-0.93; p=0.019) were associated with lower MACE. Figure 1 shows the Kaplan-Meier survival curves for the total MACEs. The four lines appear to separate early after one year, and the cumulative MACEs increase with each increase in age quartile (log-rank p=0.002).

Discussion

In this single-institute observational cohort study, we observed the following: (1) For patients who received PPCI, older age groups were associated with higher all-cause mortality. However, the differences in in-hospital mortality, recurrent MI, or any revascularization were not statistically significant after adjusting for underlying comorbidities. (2) The Kaplan-Meier survival curves demonstrated early separation of curves between Quartile 4 and the other quartiles, demonstrating increased total MACEs early after the index event in the elderly. (3) Complete revascularization and use of DES are associated with lower long-term risk of MACE, but female sex, history of stroke, CKD, and multi-vessel disease are factors associated with higher long-term risk of MACE.

Generally, short- or long-term mortality has been found to be higher in older age groups than in their younger counterparts,[8,9,11,20,21,24] In our study, the oldest age group had double the risk of

Table 1. Baseline clinical characteristics of patients divided into age quartiles

	Q1 (25 to 50 yrs)	Q2 (51 to 59 yrs)	Q3 (60 to 69 yrs)	Q4 (≥70 yrs)	P value (linear-by-linear association)
Number of patients, n	240	243	242	242	
Age, mean (years old)	44.1±5.3	55.2±2.5	64.1±3.0	77.9±5.8	< 0.001
Male, n (%)	230 (95.8)	223 (91.8)	204 (84.3)	166 (68.6)	< 0.001
Hypertension, n (%)	80 (33.3)	97 (39.9)	98 (40.5)	135 (55.8)	< 0.001
Diabetes mellitus, n (%)	37 (15.4)	57 (23.5)	67 (27.7)	68 (28.1)	0.001
Smoking, n (%)	140 (58.3)	132 (54.3)	97 (40.1)	66 (6.8)	< 0.001
Hyperlipidemia, n (%)	151 (62.9)	133 (54.7)	107 (44.2)	63 (26.0)	< 0.001
Family Hx of CAD, n (%)	6 (2.5)	5 (2.1)	1 (0.4)	0 (0.0)	0.004
Previous stroke, n (%)	4 (1.7)	7 (2.9)	14 (5.8)	18 (7.4)	0.001
CKD, n (%)	2 (0.8)	10 (4.1)	9 (3.7)	29 (12.0)	< 0.001
STEMI/NSTEMI, n (%) / n (%)	220 (91.7) / 20 (8.3)	220 (90.5) / 23 (9.5)	223 (92.1) / 19 (7.9)	216 (89.3) / 26 (10.7)	0.498
LVEF, %	53.5±11.9	52.0±12.2	52.5±12.0	52.1±13.1	0.491
LVEF < 40, n (%)	24 (10.0)	33 (13.6)	34 (14.0)	41 (16.9)	0.031
Multi-vessel disease, n (%)	97 (40.4)	111 (45.7)	130 (53.7)	144 (59.5)	< 0.001
Killip class					
1	178 (74.2)	163 (67.1)	162 (66.9)	129 (53.3)	< 0.001
2	16 (6.7)	19 (7.8)	15 (6.2)	16 (6.6)	0.804
3	3 (1.3)	13 (5.3)	7 (2.9)	17 (7.0)	0.01
4	43 (17.9)	48 (19.8)	58 (24.0)	80 (33.1)	< 0.001
Culprit vessel					
LAD	127 (52.9)	136 (56.0)	126 (52.1)	93 (38.4)	0.001
LCx	21 (8.8)	24 (9.9)	21 (8.7)	28 (11.6)	0.395
RCA	92 (38.3)	83 (34.2)	95 (39.3)	121 (50.0)	0.004
DES using, n (%)	133 (55.4)	141 (58.0)	159 (65.7)	136 (56.2)	0.482
Onset to reperfusion time, hours	4.7±3.4	4.7±3.7	4.6±3.5	5.3±5.0	0.179
Calcified lesion, n (%)	9 (3.8)	9 (3.7)	14 (5.8)	44 (18.2)	< 0.001
Complete revascularization, n (%)	176 (73.3)	172 (70.8)	148 (61.2)	134 (55.4)	< 0.001
CK-MB,	427.3±428.1	473.2±1519.7	385.2±362.0	327.2±317.4	0.321
Hs-CRP,	13.3±27.9	18.0±36.6	19.3±40.1	35.6±42.0	0.004
Total cholesterol, mg/dl	187.6±40.6	183.3±39.8	179.1±38.2	159.7±39.8	< 0.001
LDL, mg/dl	123.0±42.5	117.6±41.3	111.8±43.7	94.5±35.9	0.001

Table 2. Four years follow-up outcomes of patients post-emergency PCI by age quartile

	Patient number, n	Events, n (%)	Crude HR (95% C.I.)	P-value	Adjusted[#] HR (95% C.I.)	P-value
Recurrent MI						
Q1 (25 to 50)	240	6 (2.5)	1.00 [Reference]		1.00 [Reference]	
Q2 (51 to 59)	243	5 (2.1)	0.83 (0.26- 2.73)	0.764	0.81 (0.25-2.65)	0.724
Q3 (60 to 69)	242	12 (5.0)	2.03 (0.76-5.42)	0.156	1.93 (0.72-5.17)	0.190
Q4 (>=70)	242	10 (4.1)	1.78 (0.65-4.89)	0.265	1.53 (0.55-4.26)	0.418
Any revascularization						
Q1 (25 to 50)	240	28 (11.7)	1.00 [Reference]		1.00 [Reference]	
Q2 (51 to 59)	243	29 (11.9)	1.05 (0.62- 1.76)	0.864	1.05 (0.63-1.77)	0.850
Q3 (60 to 69)	242	36 (14.9)	1.33 (0.81- 2.18)	0.259	1.19 (0.72-1.95)	0.503
Q4 (>=70)	242	21 (8.7)	0.84 (0.48-1.47)	0.536	0.69 (0.38-1.23)	0.208
In-hospital mortality						
Q1 (25 to 50)	240	5 (2.1)	1.00 [Reference]		1.00 [Reference]	
Q2 (51 to 59)	243	6 (2.5)	1.19 (0.36-3.90)	0.774	0.75 (0.22- 2.54)	0.647
Q3 (60 to 69)	242	6 (2.5)	1.22 (0.37- 3.98)	0.747	0.72 (0.22- 2.42)	0.599
Q4 (>=70)	242	18 (7.4)	3.73 (1.39- 10.1)	0.009	1.31 (0.45- 3.80)	0.620
All-cause mortality						
Q1 (25 to 50)	240	6 (2.5)	1.00 [Reference]		1.00 [Reference]	
Q2 (51 to 59)	243	10 (4.1)	1.67 (0.61- 4.59)	0.323	1.32 (0.48- 3.64)	0.597
Q3 (60 to 69)	242	15 (6.2)	2.56 (0.99-6.59)	0.052	1.84 (0.70-4.81)	0.214
Q4 (>=70)	242	46 (19.0)	8.21 (3.51-19.2)	< 0.001	3.83 (1.56-9.37)	0.003
MACEs						
Q1 (25 to 50)	240	35 (14.6)	1.00 [Reference]		1.00 [Reference]	
Q2 (51 to 59)	243	40 (16.5)	1.15 (0.73- 1.81)	0.547	1.08 (0.69- 1.71)	0.735
Q3 (60 to 69)	242	51 (21.1)	1.50 (0.98-2.31)	0.065	1.32 (0.85- 2.04)	0.212
Q4 (>=70)	242	65 (26.9)	2.04 (1.35- 3.07)	0.001	1.42 (0.93- 2.18)	0.109

[#] Adjusted for clinical variables including sex, hypertension, diabetes mellitus, hyperlipidemia, smoking, family history of coronary artery disease, previous stroke, left ventricular ejection fraction < 40, multi-vessel disease, calcified lesion, Killip class 3 or 4, chronic kidney disease, STEMI or not, culprit lesion at the left anterior descending artery or not, use of drug-eluting stent or not, and onset to reperfusion time >12 hours in the Cox proportional regression model.

* indicates *p*-value < 0.05

Definition of MACEs: Composite of myocardial infarction, revascularization, and all-cause mortality after index PCI during 4 years.

C.I., confidence interval; MACEs, major adverse cardiac events; MI, myocardial infarction.

Table 3. Predictors of clinical outcomes in multivariable analysis

	Adjusted HR (95% C.I.)	P-value
Female gender	1.49 (1.05-2.12)	0.025
Previous stroke	2.29 (1.41-3.74)	0.001
CKD	2.98 (1.92-4.64)	< 0.001
Multi-vessel disease	1.52 (1.01-2.29)	0.045
Use of DES		
0.68 (0.51 – 0.90)	0.008	
Complete revascularization	0.63 (0.43-0.93)	0.019

[#] Adjusted for clinical variables including age, sex, hypertension, diabetes mellitus, hyperlipidemia, smoking, family history of coronary artery disease, previous stroke, left ventricular ejection fraction < 40, multi-vessel disease, calcified lesion, Killip class 3 or 4, chronic kidney disease, STEMI or not, culprit lesion at the left anterior descending artery or not, use of drug-eluting stent or not and onset to reperfusion time >12 hours in the Cox proportional regression model.

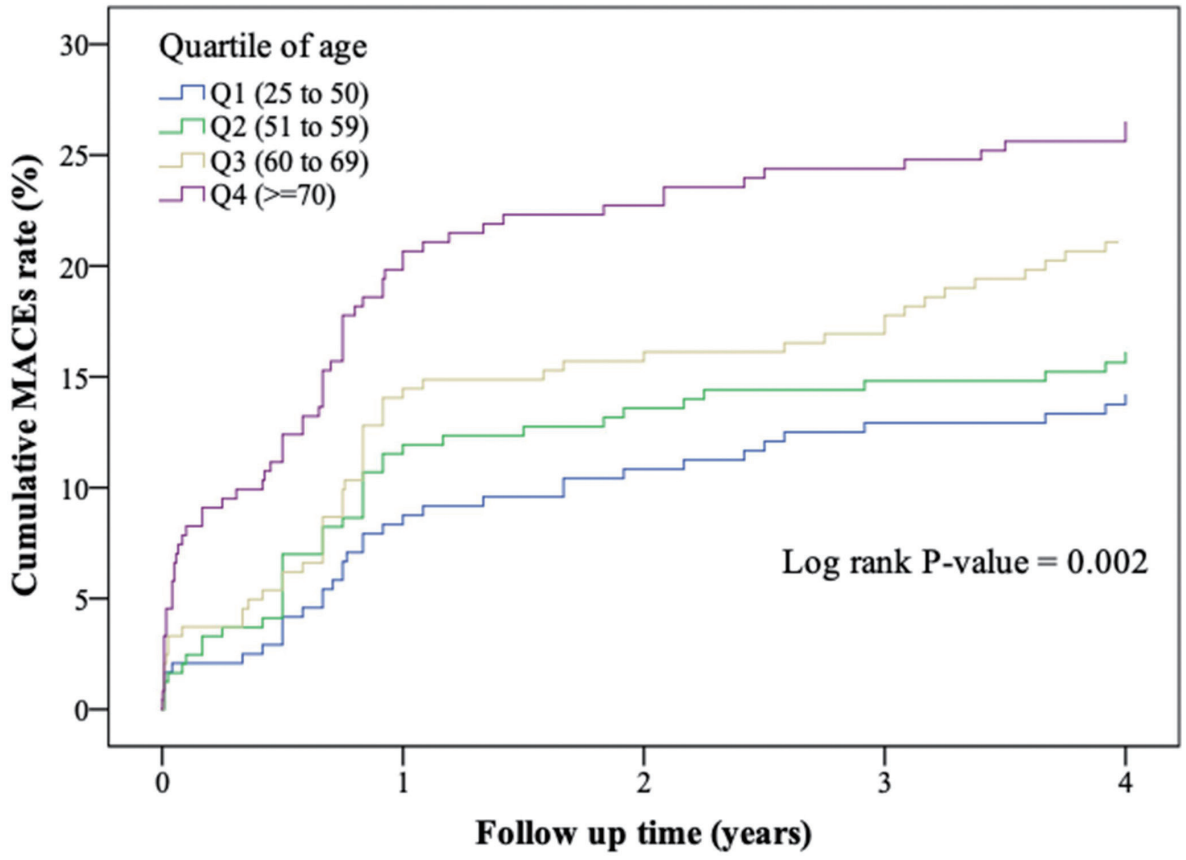

Figure 1. Kaplan-Meier survival curve of total MACEs by age quartile.

total MACE, compared to the youngest age group (26.9% vs. 14.6%). The reason for this is likely multifactorial. Elderly patients have a higher proportion of comorbidities, such as hypertension, diabetes mellitus, history of stroke, and CKD, as other studies have shown.[9,19,25] Baseline risk factors such as heart failure, complex coronary anatomy, and presentation with cardiogenic shock also increase with age.[5,6,19,25] Late presentation and longer reperfusion time are also possible causes of higher mortality in elderly patients.[6] Previous data have shown that for every 30 minutes of delay in the door-to-balloon time, the risk of 1-year mortality increased by 7.5%.[26] All of the above reasons explain the higher MACE rate in elderly patients. Interestingly, after adjusting for these characteristics, we found that age was no longer an independent predictor of MACE. The risks of recurrent MI, in-hospital mortality, and revascularization did not differ significantly among the four age quartiles. Our study seems to show a better outcome for elderly patients despite the high incidence of cardiogenic shock as a presentation.[11,24] Thus, we thought that elderly patients had reasonable chances of better short- and long-term MACE outcomes if treated properly. Outcomes research has revealed that the elderly are treated less effectively and those aged 75 years or older are less likely to receive revascularization.[27-29] Some studies have reported under-use of DES in the elderly population,[9,11,13] despite the fact that DES has demonstrated superiority over bare metal stents in clinical results.[30,31] The higher proportion of DES use in our study may also explain the better outcomes in our elderly quartile group than in previous reports.[11,27-29] To reduce ischemia time, the rate of cardiogenic shock and stent thrombosis, prompt initiation of therapy and revascularization with DES is recommended for elderly patients, as it reduces infarct size and adverse clinical consequences.[8,16] Age itself should not be a factor limiting revascularization strategies.

Patients aged 25-50 constituted 25% of the population in our study, which is similar to previous STEMI studies.[21] Most of the young patients were male (95.8%) and had a history of smoking (58.3%) or hyperlipidemia (62.9%). A family history of premature CAD was more common in the young patients than in the older patients. We also observed significantly higher rates of left anterior descending artery-related infarcts in older patients, which is similar to the findings of Rathod et al.[20] A very high prevalence of multi-vessel disease in young patients (40.4%) was observed in our study.[21]

Another finding is that previous stroke, although underrepresented in this cohort study (4.4% of the total), is associated with a significantly poorer prognosis, which may suggest that fragility, cognitive impairment, and severe dependence, rather than age, are important factors that need to be taken into consideration when deciding for emergent coronary intervention. Pajjuru et al. reported that the presence of dementia and other neurological comorbidities is associated with decreased utilization of PPCI as well as high in-hospital mortality.[16] The occurrence of acute myocardial infarction may cause a large decline in function and increase the dependency level in these patients, causing further mortality.[32] After PPCI in these patients, the daily care routine should include early cooperation with a rehabilitation doctor and initiate a cardiac rehabilitation program to prevent further functional decline. In our study, female sex was negatively correlated with survival (adjusted hazard ratio (HR): 1.49; 95% CI: 1.05-2.12; p=0.025, Table 3). This result is consistent with previous studies,[9,25,33] although not without controversy.[34]

Up to half of our patients presented with multivessel disease (49.8%) in this emergent PCI setting. The oldest age group (Q4) had the highest proportion (59.5%, p<0.001) of multivessel disease, but they were less likely to receive complete revascularization, compared to the other groups (55.4%, p<0.001). Age is possibly a concern for cardiologists when considering the degree of aggressiveness of an intervention. The

benefits and safety of complete revascularization have been well established before.[35-39] However, sub-group analyses based on age differences have shown varied results. The COMPLETE trial had the largest number of patients with a relatively longer follow-up duration, and subgroup analysis showed significant MACE reduction in both those aged < 65 years and those aged ≥ 65 years.[35] In the CvLPRIT trial, patients aged ≥ 65 years benefited more from complete revascularization than did younger patients. In the DANAMI-3-PRIMULTI trial, the benefit of complete revascularization was attenuated with age. In addition, no prognostic benefit was suggested in those aged ≥ 75 years.[40] In our analysis, all groups showed significant benefits and complete revascularization was noted with respect to age. This was similar to the COMPLETE trial, which suggested that the benefit of complete revascularization may be more significant after a longer duration of follow-up to compensate for peri-procedure-related complications and may be feasible for all age groups.

This study has several limitations. (1) This was a retrospective, single-institute study that used the CAPTAIN registry database. We only included patients with successful stenting; those with heart failure, renal impairment, or multiple comorbidities were less likely to receive reperfusion therapy. There could be a risk-treatment paradox in elderly patients. (2) Data on detailed procedural characteristics such as access type, contrast volume used, and post-procedural antiplatelet medications were unavailable, which may have introduced an undetected bias. (3) There are no data on peri-procedural complications, such as renal failure, bleeding, procedure-related stroke, or infection, all of which may have age-related differences and association with the prognosis.

Conclusion

In this study, all-cause mortality was significantly higher in the older age group than in the younger age group. However, the risk of in-hospital mortality, recurrent myocardial infarction, or any revascularization was not statistically significantly different among the age groups, after adjusting for comorbidities. This suggests that prompt revascularization and other constitutional and modifiable risk factors are equally important in PPCI, as MACE is not due to age alone.

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