



Bleeding outcomes after non-emergency percutaneous coronary intervention in the very elderly

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Abstract

Background Octogenarians constitute an increasing proportion of patients presenting for non-emergency percutaneous coronary intervention (PCI). **Methods** This study evaluated the in-hospital procedural characteristics and outcomes, including the bleeding events of 293 octogenarians presenting between January 2010 and December 2012 for non-emergency PCI to a single large volume tertiary care Australian center. Comparisons were made with 293 consecutive patients aged less than or equal to 60 years, whose lesions were matched with the octogenarians. **Results** Non-ST elevation myocardial infarction was the most frequent indication for non-emergency PCI in octogenarians. Compared to the younger cohort, they had a higher prevalence of co-morbidities and more complex coronary disease, comprising more type C and calcified lesions. Peri-procedural use of low molecular weight heparin (LMWH; 1.0% vs. 5.8%; $P < 0.001$) and glycoprotein IIb/IIIa inhibitors (2.1% vs. 9.6%; $P < 0.001$) was lower, while femoral arterial access was used more commonly than in younger patients (80.9% vs. 67.6%; $P < 0.001$). Overall, there was a non-significant trend towards higher incidence of all bleeding events in the elderly (9.2% vs. 5.8%; $P = 0.12$). There was no significant difference in access site or non-access site bleeding and major or minor bleeding between the two cohorts. Sub-analysis did not reveal any significant influence on bleeding rates by the use of LMWH, glycoprotein IIb/IIIa inhibitors or femoral arterial access. In addition, there were no significant differences in the rates of in-hospital mortality, stroke or acute stent thrombosis between the two groups. **Conclusions** In this single center study, we did not observe significant increases in adverse in-hospital outcomes including the incidence of bleeding in octogenarians undergoing non-emergency PCI.

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1 Introduction

The very elderly, defined as ≥ 80 years, represent an increasing population presenting for left heart catheterization and percutaneous coronary intervention (PCI), yet they remain an under-represented group in prospective clinical trials of PCI.^[1] One of the most frequent and important complications from PCI procedures remains bleeding.^[2] The risk of this has become accentuated with the use of anti-platelet and anti-thrombotic agents designed to improve ischemic outcomes after angioplasty and stenting. Post-PCI

bleeding is most commonly access-site related, although the risk of other types of major bleeding (e.g., gastrointestinal, central nervous system) is also increased after emergency and non-emergency PCI.^[3] Importantly, the occurrence of bleeding remains an important predictor of short and long-term mortality in PCI patients.^[4] Such concerns regarding post-PCI bleeding and its implications have led to the development of bleeding risk scores such as the integer-based bleeding risk score,^[4] the CRUSADE bleeding risk score,^[5] and the National Cardiovascular Data Registry (NCDR) bleeding risk score,^[6] designed to identify patients at increased bleeding risk and guide PCI strategy (including the use of blood-thinning agents) accordingly. All these scoring systems take into account increased age as an independent predictor of bleeding outcomes.

There is a paucity of data on bleeding outcomes after non-emergency PCI in the very elderly, as many trial protocols exclude this age group. In light of this, we set out to interrogate the patient, lesion and procedural characteristics

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as well as short-term outcomes, inclusive of bleeding, in octogenarian patients receiving non-emergency PCI, in a large volume centre in a real-world setting.

2 Methods

2.1 Patient population

All consecutive non-emergency PCI procedures (defined by those who did not require PCI within 24 h of presentation) in patients aged ≥ 80 years, at Monash Medical Centre (Clayton, Victoria, Australia) from January 2010 to December 2012, were eligible to be included for analysis. Two hundred and ninety-three very elderly patients were identified and further sub-classified by their mode of clinical presentation as either non-ST elevation myocardial infarction (NSTEMI), unstable angina, stable angina or silent ischemia. We compared these patients with a lesion matched control group composed of two hundred and ninety-three consecutive patients, aged ≤ 60 years or below undergoing non-emergency PCI during the same time period. Patients requiring emergency PCI, including those presenting with cardiogenic shock, STEMI, or ventricular arrhythmia (ventricular fibrillation or ventricular tachycardia) were excluded from analysis.

2.2 Procedure and data collection

All data were collected by consulting our institutional PCI database into which details were entered prospectively along with the patient case records. The data collected included baseline and procedural characteristics and in-hospital outcomes comprising angiographic and procedural success, bleeding events, stent thrombosis, peri-procedural myocardial infarction (MI), cerebrovascular accidents (CVA) and death. In addition, we retrospectively determined the predicted bleeding risk for all patients based on the updated NCDR bleeding risk score.^[6] Though it was our departmental policy to evaluate the bleeding risk pre-procedure, the tool used was at the discretion of the individual operators.

All interventions were performed according to the practice guidelines for PCI at the time of enrolment. All patients received at least 100 mg of aspirin and a loading dose of either clopidogrel 300 to 600 mg, or ticagrelor 180 mg or prasugrel 60 mg before or during the procedure. Heparin (70–100 units/kg) was administered at the beginning of the procedure. Administration of glycoprotein (GP) IIb/IIIa inhibitors was at the discretion of the operator. After the intervention, all patients were prescribed aspirin 100 to 150 mg/day and either clopidogrel 75 mg/day, or ticagrelor 90 mg twice daily or prasugrel 5 mg once daily for at least 12 months.

2.3 Definitions

The very elderly cohort comprised patients aged ≥ 80 years and the young cohort patients aged ≤ 60 years. Patients included for evaluation were further identified based on their mode of presentation either with NSTEMI, unstable angina or chronic stable angina. Unstable angina was diagnosed if no biomarker was detected in the blood stream at least 6 h after the initial onset of ischemic chest pain with one or more of three principal presentations: (1) rest angina (usually lasting > 20 min); (2) new-onset (< 2 months previously) severe angina, and (3) a crescendo pattern of angina (increasing in intensity, duration, frequency, or any combination of these factors). Patients were diagnosed as having NSTEMI based on elevations in cardiac biomarkers [cardiac-specific Troponin I or muscle and creatine kinase MB fraction (CK-MB)] with one or more of the three principal presentations mentioned above with or without electrocardiographic changes of ST depression and/or prominent T-wave inversions. Patients with angina on effort of duration more than three months not responding to optimal medical therapy and presenting for PCI were classified as those with chronic stable angina.

Multi-vessel disease was defined by the presence of a $> 50\%$ lesion in \geq two major coronary arteries. Renal failure was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min per 1.73 m² according to the Modification of Diet in Renal Disease (MDRD) formula: $eGFR = 175 \times (\text{Serum Creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times 0.742$ (if female). Left ventricular systolic function was classified as normal [ejection fraction (EF) $\geq 55\%$] or abnormal (EF $< 55\%$), based on assessment by transthoracic echocardiography. Prior vascular disease included carotid, aorto-femoral or lower extremity vascular disease documented by previous radiological study or vascular intervention. Coronary artery lesion type (A/B1/B2/C) was defined according to ACC/AHA classification.^[7]

The bleeding risk of each patient was evaluated retrospectively using the updated bleeding model to predict the risk of post-procedure bleeding among patients undergoing PCI from the NCDR CathPCI registry.^[6] According to this, for each patient the presence or absence of several variables inclusive of age, body mass index, previous PCI, chronic kidney disease, gender, hemoglobin, indication of the procedure and hemodynamic status of the patient on presentation were scored. Patients with a score of < 25 were considered to be in the low risk category, those with scores between 25 and 65 were considered to be of intermediate risk and those with a score > 65 were considered to be at high risk for bleeding. The updated NCDR bleeding risk score was chosen as, unlike the other bleeding risk scores, it was

developed from patients undergoing elective PCI rather than including those who had an urgent, emergency or salvage PCI.^[6]

Several studies have shown that the rate of bleeding is dependent on the definition used.^[8] We utilized the standardized Bleeding Academic Research Consortium (BARC) definition to classify the severity of bleeding events observed.^[9] Minor bleeding was defined by BARC type 1 and 2 and major bleeding was defined by BARC type 3, 4 and 5.

Angiographic success was defined as < 20% residual stenosis in the target lesion. Procedural success was defined as angiographic success without in-hospital major complications such as death, MI, CVA, and emergency coronary artery bypass surgery (CABG). Major adverse cardiac events (MACE) were defined as death after PCI, emergency revascularization (either with CABG or repeat PCI), and nonfatal MI. MI was defined as the presence of at least two of the three following criteria: ischemic symptoms; elevation of troponin (> 5 × 99th percentile upper reference limit) in patients with normal baseline values or a rise in troponin values > 20%, if the baseline values were elevated and stable or falling; or new electrocardiographic changes compatible with MI. Death was defined as all-cause mortality. CVA was defined by onset of persistent loss of neurological function caused by an ischemic or hemorrhagic event either during or after PCI.

2.4 Statistical analysis

Baseline risk factors, clinical characteristics, clinical presentation, angiographic and lesion characteristics, procedural characteristics and in-hospital procedural outcomes and bleeding outcomes were compared between the very elderly and the young cohort. Categorical variables are expressed as number and percentages and continuous variables as mean ± SD. Categorical variables were compared with a chi-square test and continuous variables were compared with Student's *t* test. Bleeding outcomes were also analyzed among several sub-groups based on use of Low Molecular Weight Heparin (LMWH), GP IIb/IIIa inhibitors, and type of peripheral arterial access and were compared between the two groups being studied. A *P* value of < 0.05 was considered statistically significant. All statistical analysis was performed using SPSS software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

3 Results

The two groups comprised 293 patients each. Their baseline clinical characteristics are presented in Table 1. The mean ages of the two groups were 83.8 ± 3.4 and 51.5 ± 6.0

Table 1. Baseline patient characteristics of the study population.

Baseline characteristics	≥ 80 yrs (n = 293)	≤ 60 yrs (n = 293)	P-value
Age, yrs	83.8 ± 3.4	51.5 ± 6.0	
Male	162 (55.3%)	250 (85.3%)	0.0001
Smoking			
Current	6 (2.0%)	98 (33.4%)	0.0001
Ex-smoker	63 (21.5%)	87 (29.7%)	0.030
Non-smoker	224 (76.5%)	108 (36.9%)	0.0001
Diabetes mellitus	82 (28.0%)	75 (25.6%)	0.576
Hypertension	234 (79.9%)	160 (54.6%)	0.0001
Dyslipidemia	201 (68.6%)	195 (66.6%)	0.659
Family history	19 (6.5%)	98 (33.5%)	0.0001
Obesity	29 (9.9%)	46 (15.7%)	0.048
Prior PCI	91 (31.1%)	89 (30.4%)	0.929
Prior CABG	34 (11.6%)	16 (5.5%)	0.012
Prior vascular disease	76 (25.9%)	129 (44.0%)	0.0001
Renal failure	161 (54.9%)	21 (7.2%)	0.0001
LV function			
Normal	175 (59.7%)	231 (78.8%)	0.0001
Reduced	118 (40.3%)	62 (21.2%)	0.0001
Indications			
NSTEMI	124 (42.3%)	128 (43.7%)	0.803
Unstable angina	64 (21.8%)	68 (23.2%)	0.767
Stable angina	99 (33.8%)	31.1% (91)	0.537
Silent ischemia	6 (2.1%)	6 (2.0%)	1.000

Data are presented as mean ± SD or *n* (%). CABG: coronary artery bypass graft; Ex-smoker: someone who has smoked greater than 100 cigarettes in their lifetime but has not smoked in the last 28 days; LV: left ventricular; NSTEMI: non-ST elevation myocardial infarction; PCI: percutaneous coronary intervention.

years, respectively. The octogenarian group contained a higher proportion of females (45% vs. 15%; *P* < 0.001), and had a higher baseline prevalence of renal impairment, reduced LV function and prior CABG. Notably, there were no significant differences between the groups in terms of mode of clinical presentation, with NSTEMI being the commonest form of presentation, followed by chronic stable angina and unstable angina.

Baseline procedural characteristics were as summarized in Table 2. As described above, the two groups were matched for lesion coronary artery site, with the left anterior descending artery (LAD) being the most commonly treated vessel. The very elderly group had higher prevalence of single vessel disease, calcified lesions and type C lesions and a higher rate of rotational atherectomy use. Conversely, the younger cohort more often had multi-vessel disease, and underwent PCI to treat bifurcation lesions or chronic total occlusions (CTO). Other notable differences between the

Table 2. Procedural characteristics of the study population.

Lesion characteristics	≥ 80 yrs (n = 293)	≤ 60 yrs (n = 293)	P-value
Vessel disease			
Single-vessel	144 (49.2%)	85 (29.0%)	0.0001
Multi-vessel	149 (50.8%)	208 (71.0%)	0.0001
Vessel treated			
LMS	8 (2.7%)	8 (2.7%)	1.0
RIM	6 (2.0%)	6 (2.0%)	1.0
GRAFT	4 (1.4%)	4 (1.4%)	1.0
LAD	133 (45.4%)	133 (45.4%)	1.0
LCX	60 (20.5%)	60 (20.5%)	1.0
RCA	82 (28.0%)	82 (28.0%)	1.0
Lesion type	n = 294	n = 301	
A	24 (8.2%)	45 (15.0%)	0.014
B1	109 (37.1%)	129 (42.9%)	0.175
B2	76 (25.8%)	70 (23.2%)	0.522
C	81 (27.5%)	53 (17.6%)	0.005
ISR	4 (1.4%)	4 (1.3%)	0.973
Bifurcation	16 (5.5%)	50 (17.1%)	0.0001
Calcification	280 (95.6%)	20 (6.8%)	0.0001
CTO	9 (3.1%)	26 (8.9%)	0.005
IVUS	3 (1.0%)	24 (8.2%)	0.0001
Rotational atherectomy	22 (7.5%)	6 (2.1%)	0.004
Aspirin	292 (99.7%)	293 (100%)	0.317
Clopidogrel	273 (93.2%)	292 (99.7%)	0.0001
Ticagrelor	14 (4.8%)	0	0.0004
Prasugrel	4 (1.4%)	0	0.132
Post procedural LMWH	3 (1.0%)	17 (5.8%)	0.003
Post procedural unfractionated heparin	2 (0.7%)	1 (0.3%)	0.563
GP IIB/IIIA inhibitor	6 (2.1%)	28 (9.6%)	0.0002
Access site			
Radial	56 (19.1%)	95 (32.4%)	0.0003
Femoral	237 (80.9%)	198 (67.6%)	
Type of stent	n = 276	n = 293	
BMS	71 (25.7%)	58 (19.8%)	
DES	194 (70.3%)	229 (78.2%)	
POBA	11 (4.0%)	6 (2.1%)	0.085

Data are presented as n (%). BMS: bare metal stent; CTO: chronic total occlusion; DES: drug eluting stent; GP IIB/IIIA: glycoprotein IIb/IIIa inhibitor; GRAFT: venous or arterial graft to a native vessel; ISR: in stent restenosis; IVUS: intra vascular ultrasound; LAD: left anterior descending artery; LCX: left circumflex artery; LMWH: low molecular weight heparin; LMS: left main stem; POBA: plain old balloon angioplasty; RCA: right coronary artery; RIM: ramus intermedius.

two groups were that more patients in the younger group received peri-procedural LMWH, GP IIB/IIIA inhibitors and had radial artery peripheral access. Notably, the overall use of GP IIB/IIIA inhibitors in this non-emergency PCI setting was low (2.1% vs. 9.6%; $P < 0.001$). With regard to the use

of oral antiplatelet agents, our institution had only just begun to utilize the newer agents ticagrelor and prasugrel by the end of the study inclusion period and therefore the use of both medications was low, although ticagrelor was used more commonly in the elderly patients than their younger counterparts. Use of drug eluting stents (DES) versus bare-metal stents (BMS) did not differ significantly between the two cohorts, with overall use of DES being in the order of 70%–80%. The stent length (24.7 ± 12.8 vs. 26.7 ± 15.9 mm) was greater in the younger population.

The procedural and in-hospital adverse outcomes of the very elderly in comparison with those of the younger population are presented in Table 3. There were no statistically significant differences between the very elderly and young cohorts in terms of overall procedural success (elderly 75.0% vs. young 81.0%) which was mainly influenced by periprocedural enzyme elevation (19.5% vs. 16.4%), in-hospital death (1.0% vs. 0.3%), CVA (0 vs. 0), and stent thrombosis (0 vs. 0). However, contrast-induced nephropathy was more common in the very elderly (12.0% vs. 7.0%; $P < 0.05$).

The bleeding outcomes between the two cohorts and their NCDR bleeding risk scores are shown in Table 4. A significantly higher proportion of the very elderly were classified as having a high risk of bleeding as per the updated bleeding NCDR score (NCDR score > 65: 61.0% vs. 4.1%; $P < 0.001$). Although the mean NCDR score in octogenarians was 69.3 ± 18.4 compared to 32.3 ± 16.6 in the younger cohort, the incidence of all observed bleeding events was not statistically different between the two groups (9.2% vs. 5.8%), nor were there significant differences for major bleeding rates (2.0% vs. 1.3%) and minor bleeding rates (7.2% vs. 4.5%). Despite trends toward higher bleeding rates in the very elderly in specific subgroups, statistical comparisons between the elderly and the young were not significant for bleeding in patients who received LMWH (25.0% vs. 5.9%), GP IIB/IIIA inhibitors (16.7% vs. 12.0%), or among those whose access site was femoral (10.1% vs. 7.6%) or radial (5.4% vs. 2.1%). The mean duration of

Table 3. Procedural outcomes of the study population.

Procedural outcomes	≥ 80 yrs (n = 293)	≤ 60 yrs (n = 293)	P-value
Peri procedural enzyme elevation	57 (19.5%)	48 (16.4%)	0.332
Procedural Success	219 (75.0%)	237 (81.0%)	0.091
Death	3 (1.0%)	1 (0.3%)	0.616
CVA	0	0	1.0
Stent thrombosis	0	0	1.0

Values are n (%). CVA: cerebrovascular accident.

Table 4. Bleeding outcomes of the study population.

Bleeding outcomes	≥ 80 yrs (n = 293)	≤ 60 yrs (n = 293)	P-value
NCDR score			
< 25	0	88 (30.0%)	0.0001
25–65	114 (39.0%)	193 (65.9%)	0.0001
> 65	12 (61.0%)	179 (4.1%)	0.0001
BARC bleeding			
0	266 (90.8%)	276 (94.2%)	0.158
1	21 (7.2%)	10 (3.5%)	0.065
2	0	3 (1.0%)	0.247
3a	4 (1.3%)	1 (0.3%)	0.369
3b	2 (0.7%)	3 (1.0%)	0.653
4	0	0	1.0
5	0	0	1.0
All bleeding	27 (9.2%)	17 (5.8%)	0.158
Access site bleeding	20 (74.7%)	11 (64.7%)	0.746
Non-access site bleeding	7 (25.3%)	6 (35.3%)	
Mortality among those with bleeding	0	0	1.0
Bleeding among patients receiving LMWH	25.0%	5.9%	0.822
Bleeding among patients receiving GP IIb/IIIa inhibitors	16.7%	12.0%	0.681
Bleeding among those with femoral access site	10.1%	7.6%	0.448
Bleeding among those with radial access site	5.4%	2.1%	0.543

Values are presented as *n* (%) or %. BARC: bleeding academic research consortium; GP IIb/IIIa inhibitors: glycoprotein IIb/IIIa inhibitor; LMWH: low molecular weight heparin; NCDR: National Cardio Vascular Data Registry.

hospital stay was 4.4 days in the very elderly compared to 3.3 days in the younger cohort ($P < 0.01$). Neither univariate nor multivariate analysis identified any predictors of bleeding in elderly patients (Table 5).

4 Discussion

This study represents a single center, real-world experience of in-hospital and bleeding outcomes in octogenarians undergoing non-emergency PCI. Our study shows that although the bleeding risk as defined by validated scoring systems is higher in this complex subset of patients, bleeding outcomes in comparison with those less than sixty years were not significantly different. Our results indicate that non-emergency PCI in octogenarians can be performed effectively and safely.

Octogenarians constitute an increasing proportion of patients presenting for PCI for stable angina and acute coronary syndromes.^[10] By comparison to optimal medical therapy, revascularization of coronary artery stenoses in the very elderly has been shown to translate to better absolute reduction in all-cause mortality compared to the younger cohort (11.0% vs. 1.8%).^[11] Despite this, elderly patients, particularly those with multiple co-morbidities, are poorly represented in clinical trials and several studies have reported that the use of invasive cardiac procedures declines

Table 5. Univariate and multivariate analysis for predictors of bleeding.

Variable	P-value	Beta co-efficient
Univariate analysis		
Age group	0.155	1.676
Gender	0.974	1.013
Diabetes mellitus	0.680	0.842
Hypertension	0.120	1.950
Total cholesterol	0.072	2.282
Obesity	0.490	0.653
Prior vascular disease	0.443	1.318
Access site (femoral vs. radial)	0.129	2.118
Body mass index	0.155	1.026
GP IIb IIIa inhibitor	0.428	1.652
Bifurcation	0.232	1.754
Calcification	0.350	1.394
Chronic total occlusion	0.996	0.996
Impaired renal function	0.230	1.737
Multivariate analysis		
Impaired renal function	0.464	1.467
Age group	0.367	1.796
Hypertension	0.503	1.394
Total cholesterol	0.205	1.879
Access Site	0.163	2.014
Bifurcation	0.100	2.273
Calcification	0.601	0.735

as patients get older.^[12–14] There may often be reluctance from clinicians to use an invasive strategy to treat coronary artery disease in the very elderly due to a perceived higher risk of complications.^[15] Recently, a randomized controlled multicenter trial (After Eighty Study) found a significant reduction in a composite clinical endpoint when octogenarians with acute coronary syndrome were managed with an early invasive strategy rather than by conservative medical management.^[16]

Elderly patients in our study had more co-morbidities compared to the younger cohort, which is consistent with several previous studies.^[17–20] We found that more octogenarians treated with PCI were women, had prior CABG, renal disease, and abnormal left ventricular function, whereas more patients in the younger cohort were smokers, had a positive family history and were obese.

4.1 Procedural and bleeding outcomes in the very elderly

Age is an important predictor of procedural outcome after PCI. Batchelor *et al.*^[17] evaluated the outcome trends in the elderly after PCI and showed that there was a declining trend in major adverse events during their four-year study period among octogenarians, though their procedural success rates (84.0% vs. 89.0%; $P < 0.001$) were relatively lower and major adverse cardiac events (4.9% vs. 1.9%; $P < 0.001$) relatively higher compared to younger patients.

Bleeding events are common and have been reported to occur in 2.2% to 14% of patients undergoing PCI.^[17,21,22] These events have been associated with increases in short- and long-term mortality, nonfatal MI, stroke and length of hospital stay.^[17,21–27] Factors which predict bleeding complications include age, mode of presentation, and comorbidities such as renal disease and congestive heart failure.^[28,29] In our study, there was no significant difference in overall bleeding rates, major and minor bleeding between the two groups being studied. This could be for several reasons. Firstly, our study was done on patients presenting for non-emergency PCI. Several risk algorithms evaluating post-PCI bleeding clearly indicate that the risk of bleeding is higher after an emergency PCI (e.g., for STEMI) compared to non-emergency PCI. Secondly, as per hospital protocol, the use of bleeding risk score was encouraged for all PCI procedures though the tool used was left to the operator's discretion. It has been shown previously that pre-procedural estimation of bleeding risk may reduce bleeding complications after PCI, especially for patients considered intermediate or high risk.^[30] Thirdly, LMWH and GP IIb/IIIa inhibitors were used less frequently in our study in octogenarians. Finally, as with most previous studies evaluating octoge-

narians, the possibility that our small sample size resulted in the observed statistical non-significance cannot be excluded. Thus, we believe that with appropriate case selection as described above, non-emergency PCI can be performed in the very elderly with bleeding rates comparable to the younger population. Also, there was no significant difference in bleeding rates between old and young cohorts even among subgroups receiving LMWH or GP IIb/IIIa inhibitors. Although this statistical non-significance may have been due to small study numbers, lower than expected bleeding rates have also been reported by other investigators in the setting of vigilant anticoagulant use.^[23]

Although the overall usage of radial access was relatively low in our study, especially in the very elderly (19.1% vs. 32.4%), there was no significant difference between the overall bleeding and access-site bleeding rates between old and young. Moreover, in subgroup analysis, bleeding was not significantly different between the young and old for either radial or femoral approach, although once again this may have been influenced by relatively small sample sizes. Although radial artery access has been found to be associated with a significant reduction in access site bleeding, it is still being less frequently implemented in patients who are at higher risk of such complications.^[31] Trans-radial catheterization in the elderly may be difficult because of a higher incidence of radial and brachiocephalic trunk tortuosity or stenosis of the upper limb artery in these patients.^[32] Also heavier calcification burden, more advanced atherosclerosis and tortuosity of the aorta and subclavian arteries may make trans-radial procedures in the elderly challenging.^[33] These technical challenges encountered during the radial approach may discourage interventionists from adopting it.^[34] It remains to be seen if the greater implementation of trans-radial access for PCI, along with use of newer anti-thrombotics (e.g., bivalirudin) which may have different safety profiles, further affects bleeding outcomes in this group of patients.

It has been previously reported that access site injury, stroke and mortality are higher in octogenarians than those < 60 years after emergency PCI.^[20] However, in our study stroke, bleeding rates, and mortality after non-emergency PCI were not significantly different between the two groups. Our data support the findings of the After Eighty Study in which no significant differences in stroke and mortality rates were observed between those elderly patients who had an early invasive strategy or conservative non-invasive approach to their management.^[16] These data indicate that anxieties about referral of elderly patients for PCI due to concerns about complications may be overstated, and suggests that timely intervention in these patients would offer

benefits which would potentially outweigh the risks secondary to the procedure. It reassures that invasive management can be done in octogenarians without compromising safety.^[35] This is especially so, as although octogenarians present with a higher risk profile, they paradoxically have been shown to have a greater absolute risk reduction with revascularization compared to younger patients.^[36]

In summary, there may be ongoing perception that PCI in the very elderly should be deferred because of co-morbidities and predicted high rates of adverse outcomes. The published data indicate that elderly patients have a greater risk reduction from revascularization than do younger patients. Many of the treatment modalities have been evaluated in younger patients in clinical scenarios that are not altogether representative of real-world scenarios, where the very elderly represent a significant and growing proportion of our interventional cases. Our data show that despite co-morbidities and high predicted bleeding scores, low bleeding rates and overall satisfactory short-term outcomes can be achieved in the very elderly in real-world PCI practice. We suspect that judicious use of bleeding score systems to rationalize the use of certain blood-thinning medication helps to keep bleeding rates at an acceptable level. Our cohort represents a distribution of non-emergency PCI cases, with a good representation of early PCI procedures for NSTEMI and unstable angina [acute coronary syndrome (ACS)] and also for elective stable angina. Acknowledging the important limitations of small sample size and retrospective analysis, our data indicate that elective and ACS-PCI can be performed with similar bleeding outcomes and adverse events in the very elderly as with the young, despite the very elderly having complex lesion characteristics.

4.2 Study limitations

Firstly, this is a single center, retrospective study, investigating a relatively small sample size. Secondly, the bleeding episodes were site-reported which might result in underestimation of actual bleeding rates. Thirdly, it is possible that patients with elective PCI may have been discharged early before recognition of bleeding complications. Fourthly, as with any retrospective analysis, there is a potential for unmeasured confounders. Randomized controlled trials addressing bleeding outcomes in the very elderly population are needed in the future. Also, we could not account for the sheath size, time when the sheaths were removed, duration of manual compression, or use of vascular closure device, each of which has the potential to influence post-procedural bleeding. Finally, the current study has not reported long-term follow-up data.

4.3 Conclusion

In this single center study we did not observe significant increases in adverse in-hospital outcomes including the incidence of bleeding in octogenarians undergoing non-emergency PCI. This confirms that PCI in this at risk cohort has an acceptable safety profile.

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References

- 1 Lee PY, Alexander KP, Hammill BG, *et al.* Representation of elderly persons and women in published randomised trials of acute coronary syndromes. *JAMA* 2001; 286: 708–713.
- 2 Mehta RH, Granger CB, Alexander KP, *et al.* Reperfusion strategies for acute myocardial infarction in the elderly: benefits and risks. *J Am Coll Cardiol* 2005; 45: 471–478.
- 3 Mehta SK, Frutkin AD, Lindsey JB, *et al.* Bleeding in patients undergoing percutaneous coronary intervention. The development of a clinical risk algorithm from the National Cardiovascular Data Registry. *Circ Cardiovasc Interv* 2009; 2: 222–229.
- 4 Mehran R, Pocock S, Nikolsky E, *et al.* Impact of bleeding on mortality after percutaneous coronary intervention. *J Am Coll Cardiol Intv* 2011; 4: 654–664.
- 5 Subherwal S, Bach RG, Chen AY. Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) bleeding score. *Circulation* 2009; 119: 1873–1882.
- 6 Rao SV, McCoy LA, Spertus JA, *et al.* An updated bleeding model to predict the risk of post-procedure bleeding among patients undergoing percutaneous coronary intervention. *J Am Coll Cardiol Intv* 2013; 6: 897–904.
- 7 Ryan TJ, Faxon DP, Gunnar RM, *et al.* Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). *Circulation* 1988; 78: 486–502.
- 8 Rao SV, O'Grady K, Pieper KS, *et al.* A comparison of the clinical impact of bleeding measured by two different classifications among patients with acute coronary syndromes. *J Am Coll Cardiol* 2006; 47: 809–816.

- 9 Mehran R, Rao SV, Bhatt DL, *et al.* Standardized bleeding definitions for cardiovascular clinical trials. a consensus report from the bleeding academic research consortium. *Circulation* 2011; 123: 2736–2747.
- 10 Garrett N, Martini EM. The boomers are coming: a total cost of care model of the impact of population aging on the cost of chronic conditions in the United States. *Dis Manag* 2007; 10: 51–60.
- 11 Devlin G, Gore JM, Elliott J, *et al.* Management and 6-month outcomes in elderly and very elderly patients with high-risk non-ST-elevation acute coronary syndromes: The Global Registry of Acute Coronary Events. *Eur Heart J* 2008; 29: 1275–1282.
- 12 Avezum A, Makdisse M, Spencer F, *et al.* Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J* 2005; 149: 67–73.
- 13 Hasdai D, Holmes DR Jr, Criger DA, *et al.* Age and outcome after acute coronary syndromes without persistent ST-segment elevation. *Am Heart J* 2000; 139: 858–866.
- 14 Yusuf S, Flather M, Pogue J, *et al.* Variations between countries in invasive cardiac procedures and outcomes in patients with suspected unstable angina or myocardial infarction without initial ST elevation. OASIS (Organisation to Assess Strategies for Ischaemic Syndromes) Registry Investigators. *Lancet* 1998; 352: 507–514.
- 15 Rajani R, Lindblom M, Dixon G, *et al.* Evolving trends in percutaneous coronary intervention. *Br J Cardiol* 2011; 18: 73–76.
- 16 Tegn N, Abdelnoor M, Aaberge L, *et al.* Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial. *Lancet* 2016; 387: 1057–1065.
- 17 Batchelor WB, Anstrom KJ, Muhlbaier LH, *et al.* Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: results in 7,472 octogenarians. National Cardiovascular Network Collaboration. *J Am Coll Cardiol* 2000; 36: 723–730.
- 18 Moreno R, Salazar A, Banuelos C, *et al.* Effectiveness of percutaneous coronary intervention in nonagenarians. *Am J Cardiol* 2004; 94: 1058–1060.
- 19 Walsh SJ, McAuley K, Johnston PW. Percutaneous coronary intervention in the elderly. *Ulster Med J* 2007; 76: 18–21.
- 20 Feldman DN, Gade CL, Slotwiner AJ, *et al.* Comparison of outcomes of percutaneous coronary interventions in patients of three age groups (< 60, 60 to 80, and > 80 years) (from the New York State Angioplasty Registry). *Am J Cardiol* 2006; 98: 1334–1339.
- 21 Kinnaird TD, Stabile E, Mintz GS, *et al.* Incidence, predictors, and prognostic implications of bleeding and blood transfusion following percutaneous coronary interventions. *Am J Cardiol* 2003; 92: 930–935.
- 22 Lauer MA, Karweit JA, Cascade EF, *et al.* Practice patterns and outcomes of percutaneous coronary interventions in the United States: 1995 to 1997. *Am J Cardiol* 2002; 89: 924–929.
- 23 Popma JJ, Satler LF, Pichard AD, *et al.* Vascular complications after balloon and new device angioplasty. *Circulation* 1993; 88 (4Pt 1): 1569–1578.
- 24 Manoukian SV, Feit F, Mehran R, *et al.* Impact of major bleeding on 30-day mortality and clinical outcomes in patients with acute coronary syndromes: an analysis from the ACUITY Trial. *J Am Coll Cardiol* 2007; 49: 1362–1368.
- 25 Aronow HD, Peysers PA, Eagle KA, *et al.* Predictors of length of stay after coronary stenting. *Am Heart J* 2001; 142: 799–805.
- 26 Cohen DJ, Lincoff AM, Lavelle TA, *et al.* Economic evaluation of bivalirudin with provisional glycoprotein IIB/IIIa inhibition versus heparin with routine glycoprotein IIB/IIIa inhibition for percutaneous coronary intervention: results from the REPLACE-2 trial. *J Am Coll Cardiol* 2004; 44: 1792–1800.
- 27 Lopes RD, Alexander KP, Manoukian SV, *et al.* Advanced age, antithrombotic strategy, and bleeding in non-ST-segment elevation acute coronary syndromes: results from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. *J Am Coll Cardiol* 2009; 53: 1021–1030.
- 28 Feit F, Voeltz MD, Attubato MJ, *et al.* Predictors and impact of major hemorrhage on mortality following percutaneous coronary intervention from the REPLACE-2 trial. *Am J Cardiol* 2007; 100: 1364–1369.
- 29 Doyle BJ, Ting HH, Bell MR, *et al.* Major femoral bleeding complications after percutaneous coronary intervention: incidence, predictors, and impact on long-term survival among 17,901 patients treated at the Mayo Clinic from 1994 to 2005. *JACC Cardiovasc Interv* 2008; 1: 202–209.
- 30 Rao SC, Chhatrwalla AK, Kennedy KF, *et al.* Pre-procedural estimate of individualized bleeding risk impacts physicians' utilization of bivalirudin during percutaneous coronary intervention. *J Am Coll Cardiol* 2013; 61: 1847–1852.
- 31 Rao SV, Ou FS, Wang TY, *et al.* Trends in the prevalence and outcomes of radial and femoral approaches to percutaneous coronary intervention: a report from the National Cardiovascular Data Registry. *J Am Coll Cardiol Intv* 2008; 1: 379–386.
- 32 Cao Z, Zhou YJ, Zhao YX, *et al.* Transradial approach for coronary angioplasty in Chinese elderly patients. *Chin Med J (Engl)*. 2008; 121: 1126–1129.
- 33 Yokoyama N, Takeshita S, Ochiai M, *et al.* Anatomic variations of the radial artery in patients undergoing transradial coronary intervention. *Catheter Cardiovasc Interv* 2000; 49: 357–362.
- 34 Hsieh V, Jolly SS. Should radial access be the approach of choice for elderly patients? *Rev Bras Cardiol Invasiva* 2012; 20: 9–10.
- 35 Psaltis PJ, Nicholls SJ. Management of acute coronary syndrome in the very elderly. *Lancet* 2016; 387: 1029–1030.
- 36 Ragosta M. Percutaneous coronary intervention in octogenarians and the safety of glycoprotein IIB/IIIa inhibitors. *J Am Coll Cardiol* 2003; 42: 433–436.