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An overview of PCI in the very elderly

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Abstract

Cardiovascular disease, and in particular ischemic heart disease (IHD), is a major cause of morbidity and mortality in the very elderly (> 80 years) worldwide. These patients represent a rapidly growing cohort presenting for percutaneous coronary intervention (PCI), now constituting more than one in five patients treated with PCI in real-world practice. Furthermore, they often have greater ischemic burden than their younger counterparts, suggesting that they have greater scope of benefit from coronary revascularization therapy. Despite this, the very elderly are frequently under-represented in clinical revascularization trials and historically there has been a degree of physician reluctance in referring them for PCI procedures, with perceptions of disappointing outcomes, low success and high complication rates. Several issues have contributed to this, including the tendency for older patients with IHD to present late, with atypical symptoms or non-diagnostic ECGs, and reservations regarding their procedural risk-to-benefit ratio, due to shorter life expectancy, presence of comorbidities and increased bleeding risk from antiplatelet and anticoagulation medications. However, advances in PCI technology and techniques over the past decade have led to better outcomes and lower risk of complications and the existing body of evidence now indicates that the very elderly actually derive more relative benefit from PCI than younger populations. Importantly, this applies to all PCI settings: elective, urgent and emergency. This review discusses the role of PCI in the very elderly presenting with chronic stable IHD, non ST-elevation acute coronary syndrome, and ST-elevation myocardial infarction. It also addresses the clinical challenges met when considering PCI in this cohort and the ongoing need for research and development to further improve outcomes in these challenging patients.

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1 Introduction

The definition of elderly varies in different studies, and currently there is no consensus as to who should be considered elderly, though the 2002 ACC/AHA guidelines for the management of acute coronary syndromes considered patients > 75 years as an "at-risk" group.[1] In this review, individuals ≥ 80 years (octogenarians) will be referred to as very elderly, and those between 60 to 79 years as elderly. An analysis from British centers looking at patients undergoing percutaneous coronary cntervention (PCI) from 2000 until 2008 had noted a shift in terms of aging of the patient population being treated with PCI, to more patients in both the 60 to 79 year old age bracket and especially in the 80 year and above age group.[2] Here, we address the unique set of challenges and considerations that this rapidly growing group of patients present.

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2 Prevalence of coronary artery disease in the very elderly

Age is a major cardiovascular risk factor and coronary artery disease (CAD) is the most common cause of death in the elderly.[3] There has been an annual rise of more than 160,000 octogenarians in the United States, and it is predicted that this population will increase nearly fivefold by 2040.[4] Understandably, ageing of a country's population as a result of sustained low fertility, combined with increasing life expectancy is likely to continue. The main risk factor for CAD is age and its prevalence increases markedly as age increases. CAD has its greatest impact on the elderly where hospitalization and death rates are usually much higher than for younger patients. 83.0% of men and 87.1% of women aged 80 or more in the US have cardiovascular disease (CVD) and about 66% of all CVD deaths occur in people aged 75 or older.[5]

3 Coronary lesions in the very elderly

The same British analysis mentioned above also observed a significant increase in the complexity of lesions being treated in the latter part of the 2000s.[2] In their study, octogenarians represented the fastest growing group of patients undergoing PCI, and 46% of them had calcified lesions. Comparing lesion characteristics of patients aged < 80 years to those > 80 years undergoing PCI, the octogenarians had a higher prevalence of calcified lesions, tortuous lesions, ostial lesions, multi-vessel disease and left main stenosis. Interestingly, when analyzing the trends from the early part to the latter part of the decade, they also identified a significant increase in the number of octogenarians undergoing left main coronary artery PCI. Thus to summarize, their landmark report showed that: (1) there has been a significant increase in the number of octogenarians undergoing PCI; (2) octogenarians have more complex lesions compared to the younger populations; and (3) are now undergoing more complex PCI procedures than was previously the case.

4 Outcomes after PCI in the very elderly

A recent seminal report from the Mayo Clinic has shown a marked temporal switch in the causes of death after PCI from predominantly cardiac to non-cardiac causes over the past two decades.[6] This trend was seen across all age groups, in single and multivessel disease and whether PCI was done for stable angina or acute coronary syndrome (ACS). A decrease in cardiac mortality was noted independent of baseline clinical characteristics and an increase in non-cardiac mortality was observed which was associated with increased non-cardiac comorbidities.[6]

The clinical outcome of octogenarians with unprotected left main disease after PCI with drug eluting stents (DES) has also been evaluated in a large multinational registry. At a median follow-up of 1088 days, there were no difference in death, cerebrovascular accident (CVA) or myocardial infarction (MI) among octogenarians revascularized with PCI versus coronary artery bypass graft (CABG) surgery.[7] Therefore, long term outcomes after PCI in the very elderly appear to be acceptable. A systematic review of clinical studies performed to identify the health-related quality of life (HRQOL) after PCI in the elderly, which is an important measure of procedural success, showed that the elderly have significant improvements in cardiovascular well-being after PCI. The HRQOL was encouragingly found to improve for at least one year across a broad range of health domains.[8] Also the elderly with symptomatic CAD not only had improved QOL with PCI but also had similar if not greater improvement in angina burden than younger patients despite having a higher risk profile.[9,10]

5 Peri-procedural bleeding in the very elderly

The most common non-cardiac complication in patients undergoing PCI is bleeding.[11] It has been shown that peri-procedural bleeding in the elderly is associated with an increased risk of death, MI, CVA, prolonged length of hospital stay and added cost.[12–14] The detrimental effects of bleeding in the elderly are in large part because blood loss can cause harmful effects through hypovolemia, hypotension, reduced oxygen carrying capacity, drug discontinuation and blood transfusion.[15] These are generally poorly tolerated in the elderly who often have reduced left ventricular (LV) function and generalized vascular disease, including increased vascular stiffness and endothelial dysfunction.[16] As stated above, age has been identified as an independent risk factor for bleeding in patients undergoing PCI.[13] The higher incidence of bleeding and other procedural outcomes after PCI in the elderly may be due to the higher incidence of comorbidities, including more extensive atherosclerosis, hypertension and renal insufficiency, as well as their more frequent presentation with hemodynamic instability or shock and the more frequent usage of femoral arterial access.[17]

Given its clinical significance, bleeding risk stratification is a vital part of management of patients presenting for PCI. Several risk scores have been developed and validated to assess bleeding risk: the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines (CRUSADE) bleeding score,[18] the Acute Catheterization and Urgent Intervention Triage Strategy and The Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (ACUITY-HORIZONS) risk score,[19] the Acute Coronary Treatment and Intervention Outcomes Network Registry−Get With the Guidelines (ACTION Registry-GWTG) risk score,[20] and the Updated NCDR bleeding risk score.[21] Among these, only the updated NCDR bleeding risk score has incorporated patients presenting for elective PCI, the other risk scores have been developed to assess bleeding risk of ACS patients.

Nearly all studies have shown an increased risk of access site related complications and associated bleeding events in the elderly.[22] Octogenarians seem to have a higher rate of bleeding even after elective PCI.[23] It remains to be seen if increasing the adoption of radial artery access and the application of pre-procedural bleeding risk score estimation to guide anti-thrombotic strategy helps in lowering the risk of bleeding complications in the very elderly.

The transradial approach for PCI was first described to be safe and effective by Campeau,[24] with transradial coronary stenting performed shortly after by Kiemeneij.[25] Transradial catheterization in the elderly may be more difficult because of a higher incidence of radial, subclavian, brachiocephalic and aortic tortuosity, calcification and stenosis.[26,27] These technical challenges encountered during the radial approach may discourage interventionists from adopting the technique.[28] On the flip-side, advanced age itself is a significant risk factor for bleeding and other vascular access complications after PCI, and the transradial approach has been clearly shown to be associated with a low incidence of these complications compared to femoral artery access.[29] Therefore, the use of transradial access may be potentially beneficial in the elderly. It has been demonstrated that even in the emergency setting of primary PCI for ST-elevation myocardial infarction (STEMI), PCI in the very elderly can be performed transradially without significant difference in terms of reperfusion time and with reduction in bleeding complications compared to trans-femoral access despite higher incidence of peri-procedural GP IIb/IIIa inhibitor use.[30–34]

6 Antithrombotic therapy in the very elderly

The use of blood thinning agents is well known to reduce cardiovascular mortality and ischemic complications in patients undergoing PCI.[35] Although the hemostatic balance in the very elderly seems to shift towards increased clotting and decreased fibrinolysis, there are other factors in these patients, such as distinct pharmacokinetic and pharmacodynamic responses, polypharmacy resulting in drug–drug interactions and increased comorbidities, which all contribute to an increased risk of bleeding after peri-procedural antithrombotic therapy.[36]

Dual antiplatelet therapy (DAPT) is currently recommended prior to and after PCI, in all patients irrespective of age,[37] although the duration of treatment may vary according to the type of presentation (elective versus acute) and the type of stent being deployed (bare-metal versus first generation DES versus second generation DES). DAPT in the elderly compared to the younger population has the following concerns which not only influence the choice of stent during PCI, but also the mode of management of CAD: (1) higher bleeding risk; (2) concurrent warfarin therapy for atrial fibrillation, which is more common with increasing age;[38] (3) higher likelihood of requiring non-cardiac surgery in the near future after PCI; and (4) increased risk of falls.

The ACC/AHA guidelines, also applicable to the elderly, recommend the use of aspirin in patients undergoing PCI.[39] A dosage of 75 mg to 150 mg of aspirin is as effective as higher doses with lower risk of adverse effects. In patients presenting with ACS and undergoing PCI, guidelines also recommend the use of clopidogrel in addition to aspirin.[40] Prasugrel a more potent P2Y12 inhibitor in the thienopyridine drug-class was associated with a 19% relative risk reduction in ischemic events compared to clopidogrel in high risk ACS patients undergoing PCI in the TRITON TIMI 38 trial.[41] However, it was associated with a 32% increased risk of bleeding especially in the elderly (> 75 years). Hence, prasugrel is generally not recommended in patients ≥ 75 years. Ticagrelor, which belongs to another class of P2Y12 receptor antagonists, showed a greater absolute (2.8% *vs*. 1.3%) and relative reduction (17.0% *vs*. 15.0%) of ischemic end-points in elderly (> 65 years) compared to younger patients in the PLATO trial, with lower incidence the primary composite end-point of cardiovascular death, MI or CVA compared to clopidogrel (9.0% *vs*. 10.7%). There was no difference between clopidogrel and ticagrelor groups in the rates of total major bleeding or severe bleeding. This trial therefore concluded that ticagrelor may be a better option than clopidogrel for patients with ACS for whom an early invasive strategy with PCI is planned.[42]

Bivalirudin and unfractionated heparin (UFH) are the two anticoagulant options most widely used during PCI. Bivalirudin has been touted as being as effective as UFH, but with nearly half the rate of bleeding shown in several land mark studies: HORIZONS AMI[43] trial, EUROMAX[44] trial in STEMI; BAT trial[45] and ISAR-REACT 3[46] in NSTEACS. Several reports however have indicated that patients on bivalirudin may have increased risk of early stent thrombosis. With regard to the elderly, an observational study of elective PCI in 2766 octogenarians, found that bivalirudin as compared with UFH was associated with a decreased risk of in-hospital bleeding (HR: 0.41; 95%CI: 0.23–0.7) and lower rate of major adverse cardiovascular events (MACE) at 6 months (adjusted HR: 0.5; 95%CI: 0.4–0.7).[47] In addition, the ACUITY trial[48] demonstrated an absolute reduction in bleeding events with the use of bivalirudin instead of heparin which was more pronounced in the elderly. A meta-analysis of randomized controlled trials however has questioned the reduction in bleeding with bivalirudin relative to UFH.[49] Thus, further investigation is still required to confirm the purported superior safety profile of bivalirudin in the elderly, especially given its higher cost than UFH. This is particularly in the elective PCI setting and in the context of contemporary dual antiplatelet agents and increased use of radial arterial access. As it currently

stands, UFH remains the standard peri-procedural antithrombotic therapy in most centers.[50]

Guidelines for the peri-procedural usage of GP IIb/IIIa inhibitors during PCI have no modification for the elderly, although higher bleeding risk in these patients is a cause of concern.[40] Data surrounding their merits and risks in older patients are somewhat conflicting between different agents. In one study, the routine use of abciximab in elderly individuals undergoing primary PCI, while safe, was not found to be as efficacious as in the young.[51] Similarly, even after NSTEMI, abciximab when used as an adjunctive therapy in the context of PCI, was shown to be of lesser benefit in elderly patients.[52] In the case of eptifibatide, an age sub-group analysis in patients with unstable angina reported that bleeding was highest in octogenarians.[53] Another trial excluding patients with renal failure, demonstrated a greater absolute (7.2% *vs*. 1.3%) and relative (52.6 *vs*. 16.0%) benefit of eptifibatide in elderly (defined as patients older than 65 years), compared to younger patients, for reducing the combined end-point of death, MI or revascularization.[54] In contrast, another study of tirofiban use in patients with unstable symptoms, showed similar treatment effect between older and younger patients.[55] Overall, a meta-analysis review of trial data involving GP IIb/IIIa inhibitors has concluded declining benefit in ACS patients of advanced age, with their usage associated with only a 4% non-significant beneficial effect in the elderly (> 70 years) and a concerning 62% increased risk of major bleeding.[56]

In summary with respect to the general use of antithrombotic therapy, the elderly seem to experience lower efficacy and disproportionately higher rates of bleeding compared to younger patients. This reinforces the importance of judicious patient selection when implementing and choosing between adjunctive blood-thinning agents during PCI, with careful consideration required to balance the risk of bleeding complications versus benefit of reducing thrombotic events. Particular emphasis should be given to taking into account the individual patient's comorbid state, and ensuring that where applicable creatinine clearance and weight adjustment are used for determining appropriate dosing.

7 Elective PCI in the very elderly

Historically octogenarians undergoing elective PCI have consistently shown lower rates of procedural success and higher rates of complications including in-hospital mortality, stroke, vascular complications, recurrent MI, and renal failure compared to younger cohorts.[57–59] The past decade has seen the development of newer generation coronary stents, increased adoption of transradial access and several adjuvant drug therapies, which are effective at improving outcomes and reducing complications.[59–64] Several studies on elderly patients suggest that the absolute benefit of these developments may be even higher in the elderly due to their high baseline risk.[57,63] A study from the USA showed that octogenarians undergoing elective PCI have good outcomes with higher procedural success rates and minimal morbidity suggesting that PCI is a safe and effective treatment modality of stable CHD even among the very elderly patients.[64]

8 PCI for STEMI in the very elderly

Timely primary revascularization for STEMI has been proven to result in decreased mortality and morbidity compared with thrombolytic therapy or medical management alone.[65] The very elderly with STEMI are more likely to have contraindications to thrombolytic reperfusion. Eligibility for thrombolytic reperfusion appears to decline with age, and moreover the very elderly are less likely to receive reperfusion even if they are eligible. Many elderly patients present with atypical symptoms, and have a higher likelihood of death after STEMI, much of which appears secondary to arrhythmic and mechanical complications. More than half of octogenarians with STEMI experience heart failure from either diastolic or systolic dysfunction.[66] A randomized multicenter, open-label clinical trial that compared primary PCI with thrombolysis in patients with a mean age of 80 years presenting with STEMI within the first six hours of symptom onset has shown that primary PCI improved outcomes in this setting.[67] There was a substantial reduction in recurrent ischemia in the PCI arm compared to thrombolytic therapy which remained significant throughout the one year of follow-up. In addition, there were no significant differences in major bleeding or transfusion requirements between the two treatment groups, presumably because of careful dosing and monitoring of anticoagulant and antithrombotic medications.[67] The risk-to-benefit ratio therefore favors primary PCI over thrombolytic therapy in the elderly, with major benefit from the former being a reduction in re-infarction and need for target-vessel revascularization, though mortality reduction appears less robust. Thus, primary PCI appears to be the reperfusion strategy of choice in octogenarians with STEMI, with thrombolytic therapy (particularly when given early) a viable alternative when primary PCI is not available.[67]

Key studies dedicated to investigating primary PCI for STEMI in the elderly and very elderly are summarized in Table 1. The Western Denmark registry compared outcomes after primary PCI in octogenarians and nonagenarians with STEMI, and found that TIMI III flow was

Table 1. Key studies of primary PCI in the elderly and very elderly with STEMI.

Study name	Nature of study	Number of patients	Main results	Study limitations
TRIANA[67] (RCT)	PPCI *vs*. Fibrinolysis in patients ≥ 75 years	266	Primary endpoint (30-day death, re-infarction, or disabling stroke) was achieved in 18.9% of patients treated with PPCI when compared with 25.4% of the patients thrombolysed ($P = 0.43$), with no significant difference in complication like major hemorrhage, blood transfusion or renal failure. Benefits were persistent at the end of one year with a significant reduction in recurrent ischemia (0.8% *vs*. 11.9%; $P < 0.001$) in the PCI arm.	Halted prematurely due to slow recruitment. Primary endpoint underpowered. Healthier population enrolled with considerable exclusion of patients with comorbidities, limiting extrapolation to broader populations.
Western Denmark Heart Registry[68]	Analysis of octo- & Nonagenarians undergoing PPCI from health care database	1322	Annual proportion of octogenarians undergoing PPCI doubled during the study period (2002–2009). Overall 30-day mortality was 17.9%, while the 1-year cumulative mortality was 27.2% and 5-year cumulative mortality was 41.1%. Acceptable outcome with a 5-year survival of more than 50% in octogenarians and nonagenarians.	Non-randomized trial. Study focused on mortality rates, however no breakdown of cause of death provided. Other endpoints like MI, bleeding complications and renal failure after PPCI not assessed.
SENIOR PAMI[80] (RCT)	PPCI *vs*. Fibrinolysis in patients ≥ 70 years	481	PPCI was superior to thrombolytic therapy (11.6% *vs*. 18.0%, $P = 0.005$) at reducing the combined secondary endpoint of death/CVA/re-infarction at 30 days. PPCI did not reduce the primary endpoint of 30-day death or disabling stroke (11.3% *vs*. 13%, $P = 0.57$).	Study was stopped prematurely due to recruitment issues. Primary endpoint not statistically significant due to insufficient sample size.
PCAT-2[81] (Meta-analysis of 22 RCTs)	PPCI *vs*. Fibrinolysis	410 octogenarians of the 6763 patients studied	Octogenarians undergoing PPCI had a lower incidence of all-cause mortality (18.3% *vs*. 26.4%, $P = 0.04$) at 30-day follow-up compared to those who were thrombolysed.	Elderly patients included in these trials form a selected group, hence the observed favorable effects might not be fully extrapolated to the general population.

CVA: cerebrovascular accident; HF: heart failure; PAMI: primary angioplasty in myocardial infarction; PCI: percutaneous coronary intervention; PPCI: primary percutaneous coronary intervention; RCT: randomized controlled trial.

achieved in 86.3% and 83.3% of these patients, respectively. The overall 30-day cumulative mortality was 17.9%, whilst the 1-year cumulative mortality was 27.2% and 5-year cumulative mortality was 41.1%.[68] Generally, the 30-day and 1-year mortality rates in octogenarians after STEMI are higher than their younger counterparts, probably because of associated comorbidities and a higher incidence of previous IHD with subsequent left ventricular dysfunction which may contribute to unfavorable prognosis. The relative risk decrease provided by primary PCI has been found to be the same in elderly and younger patients, and therefore the absolute benefit may be greater in the elderly.[69]

9 DES versus BMS in the elderly

Drug-eluting stents (DES) have rapidly replaced bare-metal stents (BMS) for PCI treatment of CAD because of their superior capability to reduce restenosis and the need for target lesion and vessel repeat revascularization. With the establishment of DES, it was evident that DAPT had to be given for a longer time after stent implantation to avoid stent thrombosis. The greater burden of comorbid conditions in octogenarians makes them more susceptible to complications due to DAPT, while these patients also have more frequent need for interruptions of this treatment (e.g., during the peri-operative period for non-cardiac surgery). These safety concerns may be the reason why DES are used relatively less frequently in the very elderly.[70] An analysis of a historical cohort of octogenarians comparing first generation DES and BMS revealed that there was no significant relationship between the type of stent used and either mortality or occurrence of adverse clinical events at one year of follow-up.[71] A multicenter randomized trial undergoing stent placement for symptomatic patients has shown that use of second generation DES when compared with BMS reduces the incidence of MI and target vessel revascularization in the subsequent year. However, there was no impact on all-cause death, CVA, and major hemorrhage between the two groups.[72] Thus, in octogenarians with an indication of revascularization, current generation DES can be safely used, with some benefits in ischemic outcomes compared to BMS. There are emerging data indicating that for elective PCI, DAPT may be limited to as little as one or three months of continuation after second generation DES de-

ployment, so concerns about having to use prolonged DAPT in elderly patients who are at risk of bleeding may not be as great as was traditionally the case. There are also ongoing studies to determine if shorter duration of DAPT can be used after PCI on ACS cohorts with new generation DES. All of this will impact on decision making as to whether to use DES instead of BMS.

A study comparing short and long term outcomes of elderly patients undergoing stenting with those of younger patients reported a higher rate of angiographic restenosis in the elderly (47% *vs*. 28%, $P = 0.0007$). This may be due to a higher incidence of ostial lesions, triple vessel disease, calcified lesions and complex lesions in the them compared to younger patients.[73] These factors make the usage of DES often desirable in the elderly. Repeat procedures and repeat revascularization may also not be desired in the elderly, because of technical challenges due to access issues, vascular tortuosity and because of the desire to avoid resubjecting elderly patients to contrast load or risk of access bleeding.

10 PCI in non-ST elevation acute coronary syndrome

Advanced age is considered as an independent risk factor for early morbidity and mortality following non-ST elevation acute coronary syndrome (NSTEACS).[74] The very elderly have more complex coronary artery disease, more comorbidities and are more likely than younger patients to suffer complications after revascularization for NSTEACS.[75] Relatively little data is directly available for outcomes of PCI in the setting of NSTEACS in aged populations (Table 2). An analysis of 18,466 patients in the GRACE registry, of whom 16% were octogenarians showed that in-hospital outcomes inclusive of heart failure, recurrent ischemia, major bleeding and death were lower among the very elderly who had revascularization compared to those who had medical management. Furthermore, at the end of six months death, MI and MACE were significantly lower among those who underwent revascularization compared to medical therapy. Multiple logistic regression analysis confirmed the benefit of revascularization on the primary study endpoint (6-month stroke, death, MI) in the very elderly.[76] Thus it appears clear that for the very elderly with NSTEACS revascularization combined with optimal medical therapy is preferred to optimal medical therapy alone. In the absence of robust randomized clinical data on PCI treatment strategies for the very elderly, observational study results remain valuable in providing insights into the outcomes after PCI. In the Treat angina with Aggrastat and determine Cost of Therapy with an invasive or Conservative Strategy-Thrombolysis in Myocardial infarction 18 (TACTICS-TIMI 18) study,[77] elderly patients(> 75 years) treated with an early invasive approach had a significantly lower risk of death or MI at 6 months (OR: 0.44, $P = 0.02$) compared to those who were treated with a delayed conservative strategy, whereas no such difference was seen among younger patient. A consistent message that emerges is that revascularization is better than medical therapy in octogenarians presenting with NSTEACS. A few trials on outcomes of patients with NSTEACS are summarized in Table 2.

11 Future directions

In order to guide decision making and ultimately improve PCI outcomes in older patients with CAD, there is a clear need for clinical trials to be conducted that are specifi-

Table 2. Key studies of PCI in the elderly and very elderly with NSTEACS.

Study name	Nature of study	Number of patients	Main results	Study limitations
GRACE Registry[76]	PCI *vs*. medical therapy	Of the 35,512 patients enrolled 15,625 (44%) were older than 70 years.	Favorable in-hospital mortality difference for those between 70-80 years (4.3% *vs*. 6.2%, $P < 0.001$) and > 80 years (7.0% *vs*. 11%, $P = 0.001$) who underwent revascularization. Six-month combined endpoint of death, MI and stroke was reduced in those between 70–80 years (7% *vs*. 13%, $P < 0.0001$) and in those > 80 years (17% *vs*. 25%, $P < 0.0001$) who underwent revascularization.	Non-randomized observational study.
TACTICS TIMI – 18[77] (RCT)	Early invasive *vs*. conservative strategy	Of the 2220 patients analyzed, 962 were 65 years of age or older	Early invasive rather than conservative strategy in the elderly resulted in reduction in the composite incidence of death or non-fatal MI at 30 days (5.7% *vs*. 9.8%; $P = 0.019$) and at 6 months (8.8% *vs*. 13.6%; $P = 0.018$).	Lack of standardization and poor precision of available troponin assays, must be considered before putting these study results into practice.
NEW YORK Registry[82]	Early invasive *vs*. initial conservative strategy	968,542 octogenarians	Primary outcome (in-hospital mortality) was significantly lower in octogenarians who had early invasive treatment (4.7% *vs*. 8.6%, unadjusted OR 0.52; 95%CI: 0.51–0.53).	Retrospective, observational study.

MI: myocardial infarction; NSTEACS: Non-ST elevation acute coronary syndrome; PCI: Percutaneous coronary intervention; RCT: Randomized controlled trial.

cally dedicated to the very elderly population, or as a minimum randomized trials need to make a point of enrolling adequate numbers of very elderly patients with less rigid exclusion criteria, to better translate their results to current real-world practice. Possible barriers in achieving this include the perceptions that older patients have an increased risk of harm than benefit from invasive procedures, not to mention their shorter life expectancy. Secondly, incorporation of functional and symptom outcomes as a measurement of treatment effect (e.g., QOL, independent living scores, angina burden) in addition to hard endpoints such as mortality or re-infarction, should be evaluated. Therapies that provide no significant reduction in mortality can be considered in the very elderly if substantial functional benefit is conferred, and their use can be justified on the basis of patient satisfaction and benefit to wider society, including reduction of costs that result from repeat hospitalizations and long term institutional care. Although, invasive management of chronic stable IHD is associated with increased initial costs of revascularization, this has been shown to be later balanced by reduced medical practitioner charges and less symptom driven late revascularization than in elderly patients whose IHD is managed medically.[78] Similar cost-effectiveness has been demonstrated for invasive PCI management of octogenarians presenting with ACS.[79] Finally, with advancements in PCI techniques and increased adoption of hybrid surgical procedures, it must be remembered that elderly patients are the ideal targets for these minimally invasive strategies, as has become the case for the burgeoning field of percutaneous intervention in structural heart disease, most notably with transcutaneous aortic valve implantation.

12 Conclusions

Key observations regarding the use of PCI in very elderly patients, along with some practical guidelines are provided in Table 3. To summarize, we also make the following five take-home messages: (1) the frequency of octogenarians presenting for PCI continues to increase; (2) the transradial approach to PCI, although potentially more challenging in the very elderly, reduces bleeding complications and improves outcomes as compared to the femoral approach; (3) it is important to tailor antithrombotic therapy in the elderly based on individual risk assessment; (4) new generation DES in octogenarians reduces recurrent ischemic events compared to BMS; and (5) Narrowing the current gaps in our knowledge, along with advancement in technology and pharmacotherapy, will hopefully continue to enable PCI-related outcomes to be improved and the function and independence of elderly patients with symptomatic CHD to be preserved.

Table 3. Key points and practical consideration in performing PCI in the very elderly.

General	• PCI in the very elderly is associated with a decrease in cardiac mortality, significant improvement in cardiovascular well-being, HRQOL and angina burden. • Elective PCI is a safe and effective treatment modality of stable CAD, when clinically indicated. • The predominant causes of death after all types of PCI in the very elderly may now be non-cardiac in nature. • Second generation DES compared to BMS reduce the incidence of MI, TVR with no impact on all-cause mortality.
Complications	• Antithrombotic therapy is associated with lower efficacy and higher bleeding rates compared to younger patients. • Reductions in peri-procedural bleeding complications may be achieved by greater use of transradial artery access and pre-procedural bleeding risk assessment with validated scoring systems. Attention to weight and creatinine clearance is required where applicable to ensure correct dose adjustment of certain antithrombotics. • Withholding of nephrotoxic medications, attention to pre and post-procedural intravenous hydration guided by assessment of LV end-diastolic pressure recording, and judicious use of contrast may help to reduce risk of contrast-induced nephrotoxicity.
Acute coronary syndrome	• Ticagrelor may be a better option than clopidogrel for those with ACS for whom an early invasive strategy is planned, while prasugrel is contraindicated in the very elderly due to higher bleeding risk than clopidogrel. • In those presenting with NSTEACS, revascularization combined with optimal medical therapy is preferred to optimal medical therapy alone. • In NSTEACS, an early invasive approach is associated with significantly lower risk of death or MI at 6 months compared to those treated with delayed conservative strategy. • PPCI compared to thrombolysis, improves outcomes in the very elderly presenting with STEMI, and hence is the reperfusion strategy of choice. • Thrombolytic therapy (particularly when given early) remains a viable alternative when PPCI is not available.

ACS: acute coronary syndrome; BMS: bare metal stent; CAD: coronary artery disease; DES: drug eluting stent; LV: left ventricular; MI: myocardial infarction; NSTEACS: non-ST elevation acute coronary syndrome; PCI: percutaneous coronary intervention; PPCI: primary percutaneous coronary intervention; STEMI: ST elevation myocardial infarction; TVR: target vessel revascularization.

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