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Review

Percutaneous coronary intervention in the elderly

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ABSTRACT

Our population dynamics are changing. The number of octogenarians and older people in the general population is increasing and therefore the number of older patients presenting with acute coronary syndrome or stable angina is increasing. This group has a larger burden of coronary disease and also a greater number of concomitant comorbidities when compared to younger patients. Many of the studies assessing percutaneous coronary intervention (PCI) to date have actively excluded octogenarians. However, a number of studies, both retrospective and prospective, are now being undertaken to reflect the, "real" population. Despite being a higher risk group for both elective and emergency PCIs, octogenarians have the greatest to gain in terms of prognosis, symptomatic relief, and arguably more importantly, quality of life. Important future development will include assessment of patient frailty, encouraging early presentation, addressing gender differences on treatment strategies, identification of culprit lesion(s) and vascular access to minimise vascular complications. We are now appreciating that the new frontier is perhaps recognising and risk stratifying those elderly patients who have the most to gain from PCI. This review article summarises the most relevant trials and studies.

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1. Introduction

The population of the UK, and indeed most of the world, is ageing. The last 25 years have seen a significant increase in the number of people above 65 years of age [1]. Projected forecasts suggest that 23% of our population in the UK will be 65 or above by 2034 [1]. Perhaps even more interesting is the fact that the fastest population increase has been in the number of those aged 85 or over. In 1984, there were around 660,000 people in the UK aged 85 and over, by 2009 this had doubled to 1.4 million [1] and by 2034 3.5 million or 5% of the UK population are expected to be 85 years old or over [1]. This population shift will consequently have implications on the UK health budget. For example, patients aged 75 or greater not only represent one third of those hospitalised with acute ischaemic events and account for more than half of all cardiac deaths [2] but also tend to have longer hospital admissions [3]. Similar trends are observed in Europe [4] and North America [5,6].

Heart disease remains the leading cause of death for both men and women of all ages [6]. One in every 6 males and one in every 7 females in Europe will die from myocardial infarction [7] and worldwide coronary artery disease (CAD) is the single most frequent cause of death with over seven million deaths every year [8]. The prevalence of CAD is associated with increasing age. However, there have historically been surprisingly few studies on the role of percutaneous coronary intervention (PCI) in the management of ischaemic heart disease in octogenarians [9]. Illustrating this is the fact that within Europe 27–34% of all NSTEMI patients are aged 75 years or over [10,11], but less than 20% of patients aged 75 years or older were included in NSTEMI clinical trials [12]. Furthermore, if elderly patients were included into clinical trials they tended to have less comorbidity than those typically seen in "real world" clinical practice [9,13].

Registry data from the mid-1990s (1994–1997), published by Batchelor et al. [14] showed that octogenarians who underwent PCI had a two to four fold increased risk of complications when compared to younger patients undergoing similar interventions. The complications included death, myocardial infarction, stroke, renal failure, and significant bleeding. Independent predictors of procedural mortality included shock, acute STEMI, severely impaired left ventricular systolic function (EF < 35%), renal impairment, diabetes mellitus and age over 85. A striking 10 fold variation in mortality was seen in octogenarians undergoing elective PCI with the mortality of 0.7% in patient with no comorbidities and 7.2% mortality in patients with severely impaired LV function or renal insufficiency. The study, however noted an improvement in outcomes over the four-year study period [14]. There is now growing evidence that PCI in the context of either primary or elective procedure is becoming safer with improved outcomes. This improvement may be attributed to technological advancement, improvements in operator skill and experience and identifying those patients that have the most to gain. This therefore, brings the question of risk versus benefit of PCI in octogenarians and older patients to the forefront.

In this review, we aim to present current evidence regarding PCI in the elderly population in various settings such as primary PCI for ST

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elevation acute coronary syndromes (STE-ACS), non-ST elevation acute coronary syndromes (NSTE-ACS) and stable coronary heart disease.

2. Methods

We performed an extensive review of the various studies in the literature of the data available on PCI in the elderly population. The authors searched various databases (EMBASE, OVID, PUBMED) using the keywords: "percutaneous coronary intervention", "elderly", "octogenarians", "nonagenarians", "ischaemic heart disease", "coronary artery disease", "angina", and "myocardial infarction". We studied the various publications that we obtained from the search results. Full text manuscripts were obtained. Only papers where the elderly were either the primary group studied or a pre-specified subgroup, were included in this review. We did not include papers where there was no clear definition for the age limits of the elderly group. We only included papers in the English language.

3. ST elevation acute coronary syndrome (STE-ACS)

There has been a dramatic reduction in mortality of patients presenting with acute coronary syndromes (ACS) in England and Wales from 2003 to 2010, across all age groups [2,3]. Mehta et al. [15] defined elderly patients as ≥65 years of age and noted that they comprised 50% of the hospital admissions for STE-ACS, however they account for 80% of STE-ACS deaths [15]. The elderly often present with atypical symptoms and consequently this may result in delayed or missed diagnoses [16]. The elderly may also pose procedural challenges due to tortuous, calcified coronary and peripheral arteries [17]. They may also have higher operative risks secondary to greater coronary disease burden and number of coexisting comorbidities [18–20]. Therefore, these are important considerations prior to undertaking PCI in acute and elective settings.

Table 1 summarises the various studies assessing primary PCI (PPCI) in elderly patients. Studies have shown that increasing age is associated with greater in hospital and 30 day mortality [21–23] and greater adverse events including non-fatal myocardial infarction, need for revascularisation, renal failure, massive bleeding and in some studies stroke [22,24,27,30,39,40,46,48,49].

Dziewierz et al. published data from the EUROTRANSFER registry [22] that included 1650 consecutive STE-ACS patients from hospitals in seven different European countries from November 2005 to January 2007. Patients were sub-divided into different age categories: <65, 65 to 74, 75 to 84, and ≥85 years of age. The data showed patients >85 years old had greater coronary disease burden, were less likely to achieve TIMI flow grade 3 after PCI and were more likely to have procedural complications and 30-day mortality of 20.4%. However, the incidence of re-infarction and urgent revascularisation were found to be independent of age. The registry identified elderly patients were more likely to be treated conservatively after coronary angiography with 6%, 10% and 16% of patients aged 65–74, 75–84 and >85 years of age respectively being managed conservatively. This inequality wherein older patients are less likely to receive evidenced based treatments such as coronary intervention than younger patients has been previously identified [21,25,26]. Studies have also suggested that age may be a factor when deciding on the type of stent if PCI is undertaken, where the elderly were less likely to receive drug-eluting stents (DES) [22,24].

However, attitudes appear to be changing. A single centre observational study in Amsterdam [23] between 1997 and 2007, found that from a total of 4506 STE-ACS patients, 379 patents (8.4%) were octogenarians. The number of octogenarians increased and the percentage of them undergoing PPCI had increased from 4 of 113 octogenarians (3.5%) in 1997 to 51 of 579 octogenarians (8.8%) in 2007. Of note, mortality had not improved over the 11 years period with 30 day and 12 months mortality rates of 21% (81 patients) and 28% (107 patients) respectively from a total of 379 patients. Similar trends were also observed by Antonsen et al. [21], from the Western Denmark Heart Registry and by Velders et al. from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) [27].

Given the associated mortality of invasive therapy within the elderly population especially when compared to younger patients, procedural success in terms of TIMI-flow have been studied to justify an invasive treatment strategy. A retrospective selected cohort of 27 nonagenarians treated with PPCI from January 2003 to May 2012 reported procedural success of 89% and 18.5% hospital mortality rate [24]. Success was defined by all studies as TIMI flow grade ≥2 after PCI with no significant residual stenosis. Other studies have also reported similar success rates with Koutouzis et al. [28], Danzi et al. [29] Salinas et al. [30] and Singh et al. [46] reporting success rates of 82% (n = 22), 85% (n = 100), 90% (n = 38) and 92% respectively. Associated mortality rates observed were 27% [28], 19% [29] and 34.2% [30]. These studies suggest that coronary intervention is a plausible strategy for elderly patients with high success rates. However several other factors contribute to mortality and these include vascular access, bleeding risk, renal function, delays in presentation and patient frailty.

A significant factor associated with adverse prognosis, especially in the elderly population on mortality is delays in presentation [31,32]. Ionescu et al. [31] studied 24 nonagenarians presenting with STEMI, from 2004 to 2008, 13 underwent invasive therapy whereas 11 were treated medically, and demonstrated that elderly patients benefited from PPCI when presenting within 6 h when compared to medical therapy. The numbers were small but Kaplan–Meier analysis demonstrated a survival benefit favouring PPCI if patients presented within 6 h. Importantly, there was no difference in complication rates between the two groups in terms of bleeding, cerebrovascular accidents or acute renal insufficiency. This reflected findings from the GRACE registry, with delayed time to presentation being one of the most important contributors to mortality in elderly patients [32].

There is currently growing evidence of an important factor associated with prognosis — the concept of frailty. Geriatricians are now increasingly assessing frailty scores in older patients as a marker of prognosis and guide possible treatment strategies [33]. The assessment of frailty and delay in presentation is discussed in The future of PCI in older patients section.

There have been suggestions that in elderly patients would thrombolysis be a safer option than PPCI. The TRIANA study [34] compared PPCI versus thrombolysis in patients aged >75. 134 patients who were treated with PPCI with 132 patients with fibrinolysis showed improved outcome for patients treated with PPCI with a combined endpoint of death, recurrent myocardial infarction and disabling stroke at 30 days in the elderly (odds ratio 0.64; 95% C.I. 0.45–0.91). Patients that underwent PPCI also had significant improvement of recurrent ischaemia. However the trial was stopped early due to the difficulty in the slow recruitment rate. The efficacy of thrombolysis in elderly patients has also been questioned [35]. In fact, Van der Werf [36] suggested that age is the single most important risk factor for mortality in STE-ACS patients undergoing thrombolytic therapy. Elderly patients having thrombolysis also had the highest MACE rates, 3.3% of patients had intracranial haemorrhage, greater than 20% of patients requiring blood transfusion after significant bleeding, greater prevalence of cardiac rupture and heart failure [37]. Similar results were observed by Berger et al. [38]. In a subgroup analysis of patients stratified by age, the Senior Primary Angioplasty in Myocardial Infarction (SENIOR PAMI) found in patients between 70 and 80 years of age a non-significant 38% reduction in death, a non-significant 36% reduction in death/cerebrovascular accident, however a statistically significant 55% reduction in the combined end point of death/cerebrovascular accident/re-infarction. Interestingly in patients older than 80 years there was no significant advantage of either PPCI or thrombolysis [39]. The Primary Coronary Angioplasty Trial (PCAT) [40] investigators pooled 11 randomised trials of PPCI versus fibrinolytic therapy from 1989 to 1996. The study found a significantly reduced 30-day mortality or non-fatal myocardial infarction rate for all patients in the PCI group when compared to thrombolysis group, 4.3% and 6.9% respectively an effect that likely extended to 6 months. PPCI was also associated with reduced reinfarction and significant reduction haemorrhagic stroke [40]. Similar significant difference was seen in a subgroup analysis of patients >70 with mortality or nonfatal myocardial

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