**Comparison of the Effects of Incomplete Revascularization on 12-month Mortality in Patients <80 compared to ≥80 Years of Age Undergoing Percutaneous Coronary Intervention.**

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**ABSTRACT**

**Introduction:** Increasing numbers of elderly patients are undergoing percutaneous coronary intervention (PCI). However the impact of differing revascularisation strategies is not well defined. **Methods:** A retrospective analysis was conducted of all patients who underwent PCI at a large UK cardiac centre between 2008 and 2014. **Results:** During the study period 9,628 patients underwent PCI with the elderly cohort (≥80years) increasing significantly in size (5.4% in 2008 to 10.2% in 2014). Elderly patients were more likely to be female, to have significant comorbidity, a higher Mehran bleed risk score (24.5±6.8 vs. 13.3±7.4, p<0.0001), more complex disease (baseline SYNTAX score 18.7±11.0 vs. 13.1±8.9, p=0.002), and a greater incidence of proximal left coronary disease than younger patients. During PCI, the elderly were more likely to undergo left main or proximal LAD intervention but significantly more likely to receive a bare metal stent (34.5 vs. 19.9%, p<0.001). Post-procedurally the elderly cohort had greater residual disease burden (residual SYNTAX 10.1±8.7 vs. 1.6±3.3, p<0.0001) and more frequent adverse outcomes (definite stent thrombosis 2.1 vs. 3.3%, p=0.017, clinically driven ISRS-PCI 3.7 vs. 2.6%, p=0.036, and 12-month mortality 12.8 vs. 4.2%, p<0.0001). Although age, shock, low EF and diabetes were independently associated with 12-month mortality, incomplete revascularisation was not. **Conclusions:** Patients over 80 years of age have complex coronary disease but are more commonly treated with bare-metal stents. Additionally although the elderly are more likely to receive incomplete revascularisation it was not independently predictive of adverse outcomes. These data support a conservative revascularisation strategy in the elderly.

**INTRODUCTION**

As the population of the Western world progressively ages the number of elderly patients presenting with coronary artery disease also increases.A recent analysis of global cardiovascular (CV) deaths found that although there was a 40% reduction in age-specific CV mortality there was a 40% increase in the number of overall CV deaths due to the increasing age of the world’s population.1 Additionally the definition of elderly as a separate sub-group has been recently debated in light of registry evidence revealing that patients over 75 years now represent 27-34% of patients presenting with a non-ST elevation myocardial infarction (NSTEMI).2,3 However despite this increasingly larger population, data derived from multiple sources clearly demonstrates that the elderly are significantly less likely to be managed invasively and to receive revascularisation. For example in the GRACE registry, coronary angiography was performed in 67% of patients over 70 years of age compared with only 33% in patients over 80 years.4 In the same fashion in the CRUSADE registry coronary revascularisation was performed in 40.1% of patients 75–89 years of age vs. 12.6% in those ≥90 years.5 Finally in the EuroHeart survey increasing age was associated with a progressive decline in PCI rates.3,6

Although the elderly are less likely to be managed using as early invasive strategy, data from several studies including TACTICS-TIMI 18 and the German Acute Coronary Syndromes registry reveal an improvement in short and medium-term outcomes compared to a more conservative strategy in this cohort.7,8 In light of these data the most recent ESC NSTEMI guidelines recommend that elderly patients should be considered for an invasive strategy and, if appropriate, revascularization after a careful weighing up of the potential risks and benefits of such an approach.9

Although there is a robust data set defining the presentation and initial management of elderly patients presenting with coronary artery disease, data regarding the elderly patients who actually undergo PCI are less well characterised. Additionally the impact of stent choice and completeness of revascularisation on outcomes in the elderly are uncertain. Therefore in the current study we examined the baseline demographics, procedural characteristics and outcomes of a large cohort of elderly patients undergoing PCI.

**METHODS**

Our institution provides cardiac care to a population of nearly 1.5 million and performs in excess of 1,600 PCI procedures a year. To generate sufficient numbers all patients undergoing PCI in a six-year period (2008-2013) were studied. For the purposes of the current study we defined elderly as ≥80 years of age. The baseline demographics, procedural characteristics and 12-month outcomes for elderly patients undergoing PCI were then compared to younger patients (<80 years of age) undergoing PCI.

Patient demographics and procedural data were retrieved from the national British Cardiovascular Intervention Society Database (BCIS) Central Cardiac Audit (CCAD) database. The standard CCAD definitions of comorbidity were used for the study purposes. Mortality was recorded from the Welsh Demographic Service database. Repeat revascularisation data were derived from an internal angiographic database and the CCAD database. Clinical in-stent restenosis PCI (ISRS-PCI) was defined as repeat PCI to a stenosis >50% in a previously stented segment (+5mm margins) which was performed due to presentation with recurrent angina with evidence of inducible ischaemia, or presentation with an acute coronary syndrome (non-ST or ST elevation). Stent thrombosis was defined as per the ARC definite criteria.

To assess baseline bleeding risk we used the Mehran score.10 As with other studies we modified this slightly by excluding peri-procedural anti-coagulant therapy.11 Therefore we assigned a score based on sex (male=0, female=+8), age (<50=0, 50-59=+3, 60-69=+6, 70-79=+9, ≥80=+12), serum creatinine (<1.0=0, 1-1.19=+2, 1.2-1.39=+3, 1.4-1.59=+5, 1.6-1.79=+6, 1.8-1.99=+8, ≥2=+10), white blood cell count (<10=0, 10-11.99=+2, 12-13.99=+3, 14-15.99=+5, 16-17.99=+6, 18-19.99=+8, ≥20=+10), presence of anaemia (no=0, yes=+6) and presentation (STEMI=+6, NSTEMI=+2, unstable angina/elective=0). Bleeding risk based on the modified Mehran was categorised into low (<10), moderate (10-14), high (15-19) and very high (≥20).

For SYNTAX score calculation an on-line calculator was utlised (http://ir-nwr.ru/calculators/syntaxscore.htm). Score were calculated by 4 experienced interventional cardiologists who were blinded as to the patient’s age. To calculate baseline SYNTAX score the pre-PCI angiograms were assessed and scored. To calculate residual SYNTAX score the final post-PCI angiogram was scored to assess untreated disease. As with previous SYNTAX studies scores were categorised into low (<22), intermediate (23-32) and high (≥33).12

Continuous data were expressed as mean (SD) and comparison between groups was performed using Student T-Test. Categorical data are presented as frequencies and percentages, and were compared using chi-square table statistics. Binary logistic regression analysis was performed on Minitab (V16) and co-linearity was confirmed using Principal Component Analysis and inspection of Loading Plots. Multivariate logistic regression tests were run for each analysis with variables included being age, presentation, shock, previous MI, diabetes, ejection fraction, history of CVA, history of PVD, chronic kidney disease, stent type and completeness of revascularisation. Goodness-of-fit for the binary logistic regression analyses were examined using the Pearson, Deviance and Hosmer-Lemeshow tests. The results are presented as odds ratios (OR) and 95% confidence intervals. The null hypothesis was rejected at the level P<0.05.

**RESULTS**

*Baseline patient characteristics and disease severity*

9,628 patients underwent PCI with the mean age of the whole patient cohort increasing from 62.4±11.4yrs in 2008 to 64.8±11.8yrs in 2014 (Figure 1, panel A). Of the whole cohort 727 were aged ≥80 years (7.6%) with 5.4% ≥80yrs in 2008 vs. 10.2% in 2014 (p<0.0001, Figure 1, panel B). The baseline demographics of the two cohorts are presented in Table 1. Elderly patients were more likely to be female (34.8 vs. 24.6%, p<0.0001), have low body weight (BMI 25.9±4.3 vs. 28.9±5.8, p<0.0001) or to have severe LV dysfunction (12.5 vs. 6.9%, p=0.0004), more likely to have significant comorbidity including hypertension (71.5 vs. 62.8%, p<0.0001), chronic kidney disease (7.9 vs. 2.8%, p<0.0001) peripheral vascular disease (5.9 vs. 3.1%, p<0.001) or history of stroke (3.6 vs. 2.1%, p<0.05) and more likely to present with ST depression (19.6 vs. 14.3%, p=0.003) or cardiogenic shock (5.1 vs. 2.4%, p<0.0001) than younger patients. The overall and components of the modified Mehran bleed risk score are presented in Table 2. The bleed risk was significantly higher in elderly patients treated vs. younger patients (24.5±6.8 vs. 13.3±7.4, p<0.0001) with this difference being driven by all components of the score apart from white blood cell count. The breakdown into risk groups is presented in Figure 2 with 81.5% of the elderly patients categorised as very high-risk for subsequent bleeding.

The baseline coronary disease data are presented in Table 3. Elderly patients presented more often with proximal left coronary disease, with more lesions and vessels diseased, and were more likely to have a chronic total occlusion (CTO) of at least one artery. The baseline SYNTAX score was significantly greater in elderly patients vs. younger patients (18.7±11.0 vs. 13.1±8.9, p=0.002) (Figure 3A).

*PCI procedural data*

Despite the significant excess of mean number of vessels diseased in the elderly cohort (delta 0.39 vessels) there was only a small increase in the number of vessels treated (delta 0.05 vessels, p<0.0001, Table 3). Additionally although a CTO was more likely to be present in the elderly it was less likely to be treated. During PCI consistent with the anatomy and baseline characteristics the elderly were more likely to undergo left main, proximal LAD graft intervention (Table 4). However operators were more likely to resort to atherectomy use or intra-aortic balloon pump support in the elderly but less likely to utilise aspiration thrombectomy, intra-coronary imaging or a glycoprotein receptor inhibitor. Because of the slight excess of vessels treated, the elderly cohort received more stents that the younger cohort. However despite this, the increased complexity of the intervention and the greater likelihood of proximal left coronary intervention, the elderly were significantly more likely to receive a bare metal stent (34.5 vs. 19.9%, p<0.001, Table 4). Additionally, there was a close association between increasing age and BMS within the elderly cohort with the lowest use in the 80-81year old group (29.7%) and highest in the >90years group (54.8%, p<0.001 for trend). Immediate procedural success and complications were similar between the two groups.

Post-procedure, the elderly cohort had greater residual disease burden. As is demonstrated in Table 3 the number of vessels not attempted, the number of residual vessels, the likelihood of a residual CTO being present were all significantly greater in the elderly. The residual SYNTAX was also significantly higher than in younger patients (10.1±8.7 vs. 1.6±3.3, p<0.0001) (Figure 3B).

*Clinical outcome of the elderly and younger cohorts*

All clinical end-points were more likely in the elderly cohort (Table 5). ARC definite stent thrombosis (2.1 vs. 3.3%, p=0.017) and clinically driven ISRS-PCI (3.7 vs. 2.6%, p=0.036) were more frequent and 30-day (6.6 vs. 1.9%, p<0.0001) and 12-month mortality (12.8 vs. 4.2%, p<0.0001) were higher. Consistent with the incomplete revascularisation during the index procedure the elderly cohort were less likely to have further non-target vessel PCI during follow up.

The univariate associates of mortality in the elderly cohort are presented in Table 6. However using binary regression analysis only shock (OR 8.91, 4.11-19.29, p<0.001), age (OR 1.11 1.03-1.18, p=0.004), ejection fraction less than 30% (4.55, 2.41-10.0, p<0.001), and diabetes (OR 2.22, 1.23-4.01, p=0.008) were independent predictors of mortality in the whole elderly cohort (Table 7). In sub-group analysis, if shocked patients were excluded only age (OR 1.09, 1.01-1.17, p=0.037), ejection fraction less than 30% (4.20, 2.21-8.81, p=0.002), diabetes (OR 2.16, 1.15-4.07, p=0.016), and BMS use (OR 1.69, 1.00-2.12, p=0.05) were predictive of increased mortality. Incomplete revascularisation was not independently associated with adverse outcomes (with or without shock included).

**DISCUSSION**

In the current study we observed - consistent with population data - that patients over the age of 80 years represent an increasingly large cohort and account in most recent years for over 10% of all patients undergoing PCI in a high-volume interventional centre.

It is striking to observe the very significantly higher baseline SYNTAX score in older patients with the higher prevalence of several of the traditional coronary artery disease risk factors in this group as being one possible explanation for this observation. However despite the higher SYNTAX scores it is clear that operators were less likely to attempt full revascularisation. Additionally despite the increased complexity of the intervention and the greater likelihood of proximal left coronary intervention, the elderly were significantly more likely to receive a bare metal stent. This observation is consistent with a contemporary registry of bare metal stent use, in which advanced age was the commonest patient factor recorded in influencing operator stent choice.13

One possible explanation underpinning these observations is that operators were cognisant of the risks of prolonged courses of dual anti-platelet therapy in the elderly and therefore limited the numbers of stent implanted and preferred bare-metal stents where possible. The observed increase in bare metal stent as age increased within the elderly cohort is further evidence in support of this hypothesis. Elderly patients are an extremely difficult group to manage both in terms of pharmacology and revascularisation. On the one hand age is a strong predictor of adverse outcomes from ischaemia in the GRACE risk score and therefore full revascularisation would be an attractive strategy. However conversely age is also a strong predictor of bleeding in several bleeding risk scores (including CRUSADE and NCDR) and therefore with elderly are clearly at greater risk with more aggressive and more prolonged DAPT.14 Additionally newer more potent anti-platelet agents such as prasugrel were associated with even higher risks of major bleeding than clopidogrel in this cohort.15

However although bare-metal stent use is an attractive option in patients at risk of bleeding, their concomitant complex coronary disease means the risk of repeat TLR rates is likely to be high with this approach.16-18 Indeed the ZEUS study (in which more than 1600 patients were over 75 years of age were randomised) demonstrated that implantation of a zotaralimus-eluting stent with an abbreviated course of DAPT (1-month) led to superior outcomes when compared to a bare-metal stent strategy in patients who were felt to be poor candidates for prolonged DAPT.19 Additionally several recent randomised trials have shown non-inferiority with shortened DAPT duration (3-6 months) compared to standard duration (12-24 months).20-23 As a result the recent ESC guidelines on revascularisation support abbreviated DAPT duration in patients deemed to be at risk of bleeding such as the elderly.24

The partial revascularisation in elderly patients led to high residual SYNTAX scores. In the SYNTAX trial, a high residual score closely correlated with adverse outcomes after PCI.25 However in contrast to the SYNTAX trial, incomplete revascularisation in the elderly in the current study did not correlate with mortality at 12-months, with only overriding comorbidity such as shock, diabetes and low EF predictive of death. These data therefore support a conservative revascularisation strategy in the elderly with treatment of disease targeted at symptom relief only. The observation of a marginal association between bare metal stent use and adverse outcomes in the non-shocked elderly group is intriguing and hypothesis generating, and is worthy of further study. Additionally the advent of newer stent technologies may allow interventional cardiologists more freedom to minimise bare-metal stent use without fear of inducing bleeding with long courses of post-PCI DAPT. Of particular interest is the BioFreedomTM drug-coated stent (Biosensors SA, Morges, Switzerland). The rapid drug-elution profile of this stent may allow a shortened duration of DAPT without compromising TLR and MACE.26-27 In the LEADERS-FREE trial age over 75 years of age as a major inclusion criteria and the recently presented results demonstrate superior efficacy and safety over a bare-metal stent strategy.28 Similarly in the SENIOR trial the Synergy stent (Boston Scientific, Marlborough, United States) is being studied in the elderly with an ultra-short (1-month) DAPT course.29 Therefore it is fascinating to speculate that in future the accumulating evidence in support of an abbreviated DAPT course in certain high-risk groups combined with newer stent technologies may enable interventional cardiologists to undertake more effective revascularisation in the elderly which may in turn improve outcomes.

Possible limitations of the current study are firstly that the data are derived from a single center experience and therefore the patient demographics, procedural process and outcomes may not reflect typical practice in other centers. Secondly as with any registry there may be other unmeasured confounders that are influencing the results. Thirdly follow-up bleeding data were not available. However these data have been presented previously from other registries and trials, and the Mehran bleed score has been independently validated. A final limitation is that DAPT therapy (type and duration) for not recorded for our patients and if available would also provide fascinating insights into prescribing patterns and age.

In conclusion patients over the age of 80-years represent an increasingly large cohort undergoing PCI and have increased comorbidity and complex coronary disease. These patients are more likely to receive incomplete revascularisation, bare-metal stents and have adverse 12-month outcomes.

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