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Acute coronary syndromes: an old age problem

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Abstract

The increasing population in older age will lead to greater numbers of them presenting with acute coronary syndromes (ACS). This has implications on global healthcare resources and necessitates better management and selection for evidenced-based therapies. The elderly are a high risk group with more significant treatment benefits than younger ACS. Nevertheless, age related inequalities in ACS care are recognised and persist. This discrepancy in care, to some extent, is explained by the higher frequency of atypical and delayed presentations in the elderly, and less diagnostic electrocardiograms at presentation, potentiating a delay in ACS diagnosis. Under estimation of mortality risk in the elderly due to limited consideration for physiological frailty, co-morbidity, cognitive/psychological impairment and physical disability, less input by cardiology specialists and lack of randomised, controlled trials data to guide management in the elderly may further confound the inequality of care. While these inequalities exist, there remains a substantial opportunity to improve age related ACS outcomes. The selection of elderly patients for specific therapies and medication regimens are unanswered. There is a growing need for randomised, controlled trial data to be more representative of the population and enroll those of advanced age with co-morbidity. A lack of reporting of adverse events, such as renal impairment post coronary angiography, in the elderly further limit risk benefit decisions. Substantial improvements in care of elderly ACS patients are required and should be advocated. Ultimately, these improvements are likely to lead to better outcomes post ACS. However, the improvement in outcome is not infinite and will be limited by non-modifiable factors of age-related risk.

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1 Acute coronary syndromes

Current acute coronary syndrome (ACS) management is underpinned by evidence from randomised, controlled trials (RCTs). Guidelines developed by bodies such as, the European Society of Cardiology (ESC)[1,2] and the American Heart Association/American College of Cardiology (AHA/ACC),[3,4] summarise such trials to provide reliable levels of evidence and recommendations for treatment. Despite the guidelines and improved care over the last two decades, coronary heart disease (CHD) remains the leading cause of mortality in the developed world.[5]

Inequalities and variations in ACS care are well recognised, no more so than in elderly patients with ACS.[6-8] Older patients represent a significant proportion of those presenting with ACS. However, they are under represented in clinical trial data, since advanced age has been an exclusion criterion for the majority of studies. Furthermore, older patients and, more so, those with uncertain diagnoses may more frequently be placed under the care of non-cardiologists during their hospital admission. Whereas, ACS patients cared for by cardiologists, had greater rates of proven therapies and invasive investigations with lower 90-day mortality rates.[9] Therefore, the evidence base for ACS treatment may not reflect the impact (positive or negative) in the elderly population and a lack of specialist care and inappropriate placement within a hospital may, in part, explain the inequality in provision of evidence-based therapies to elderly ACS.

2 The challenges of age and ACS

Older patients have poorer outcomes than younger coun-

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terparts following an ACS.[10-17] This is related to a multitude of factors (table 1). Older age is a recognised risk factor not only for the development of CHD, but also highlighted in many ACS risk models to predict "short" and "long" term mortality,[18-21] such as the Global Registry of Acute Coronary Syndrome. Results from the Myocardial Ischemia National Audit Project, a multicentre clinical registry of patients hospitalised with ACS in England and Wales, reveal that up to 12% of patients hospitalised with an ACS were aged 85 years or older.[10] Notably, this proportion will increase with predictions of men and women born in 2009 in the UK living to 88.7 and 92.3 years old, respectively.[22] A similar pattern is seen in USA.[23,24]

However, evidence from several observational trials suggests older patients less frequently receive evidence-based ACS therapies and have higher mortality rates than their younger counterparts.[10–17] For example, in a recent study of 616,011 patients in the Myocardial Ischemia National Audit Project registry for England and Wales, patients aged 85 years or older (deemed eligible for treatment) presenting with an ST-elevation myocardial infarction (STEMI) were up to 75% less likely to receive reperfusion therapies, such as thrombolysis or primary percutaneous coronary intervention (PPCI), compared with those under 55 years of age, and less frequently received secondary prevention medication on discharge from hospital.

Table 1. Possible factors contributing to poorer outcomes in the elderly following an acute coronary syndrome.

Elderly ACS: problem list	Concerns
Decreased lean body weight and altered metabolic function	Alterations in handling and metabolism of ACS medications leading to uncertainty of effect and risk benefit decisions.
Decreased renal clearance and increased chronic renal failure	Retention of ACS medications leading to increased medication side effects, such as, significant bleeding.
Physiological, physical and cognitive decline	All impact on the presentation, treatment effects, recovery and long term management of ACS.
Increase co-morbidity and medication usage	Increased frailty and chance of complications from treatments such as drug interactions.
Increasing burden of elderly ACS	Increasing need for health resources worldwide and better management strategies.
Atypical ACS presentation	Poor recognition of ACS event and therefore inadequate risk stratification and subsequent treatment.
Lack of RCT data to represent "Real World" elderly ACS	Limited data to guide treatment of elderly ACS. Most "Real World" elderly patients are excluded from RCTs. There is an increasing need for more inclusive trials.
Receive less evidence-based treatments for ACS	As elderly ACS patients are high risk for poor outcomes, they would potentially benefit most from evidence-based treatments but continually receive less than younger counterparts.

ACS: acute coronary syndromes; RCT: randomised, controlled trials.

For example, 66.8% of patients less than 55 years of age received an angiotensin converting enzyme inhibitor (ACEi) compared with 48.8% of patients 85 years or older.[10]

Furthermore, even though hospitalised patients aged 85 years or older with ACS were less likely to smoke, they more frequently had a greater burden of co-morbidity, although females less so than males. Older patients more frequently presented to hospital admission with a non-ST-elevation myocardial infarction (NSTEMI) and less frequently had a final discharge diagnosis of STEMI. They were less likely to call the emergency services or make their own way to hospital, and more frequently had an in-hospital ACS as a presentation. In addition, more frequently they are more unstable at hospitalisation and a greater proportion were in cardiogenic shock (which significantly increased from 2003 to 2010 in all age groups) for both STEMI and NSTEMI than those < 55 years (STEMI: 5.0% *vs*. 2.1%; NSTEMI: 3.1% *vs*. 1.2%, respectively). Those 85 years or older had greater lengths of hospital stay and significantly higher in-hospital mortality rates, with the highest risk of in-hospital mortality evident for males 85 years or older with STEMI (20 fold increase in risk of death compared with males younger than 55 years with STEMI).[10] Nonetheless, risk of in-hospital mortality declined year on year for both STEMI and NSTEMI across all age groups, which remained significant following adjustment for patient-level factors.[10] There was also an improvement in the provision of evidence-based therapies, although age related inequalities were evident.

The elderly with ACS are at high risk for adverse outcomes, but those at high risk have the most to gain from ACS therapies.[10,25] There is evidence to support a reduction in the risk of mortality after ACS, and in part, this has been related to better provision of evidence-based ACS treatments.[26–28] Indeed, it is advocated that while age related inequalities in care persist, improved outcomes in the elderly suffering an ACS may translate from improved adherence to evidence-based therapies.[16]

3 Why are the elderly with ACS disadvantaged?

There are many possible reasons why the elderly hospitalised with ACS are disadvantaged. Elderly patients are more likely to present with atypical symptoms (for example, presenting without chest pain) as illustrated by a study where 8.4% of patients with ACS presented atypically (49% dyspnoeic, 28% diaphoretic, 24.3% nauseated and 19.1% syncopal or pre-syncope) and were significantly older than those typically presenting.[29] Furthermore, initial electrocardiograms (ECG) are less likely diagnostic of ACS, with frequent delays to first ECG,[23] and presentation with STEMI (which typically

is clinically more apparent than NSTEMI) is less likely.[10,24] This may lead to uncertainty about the initial diagnosis and potentially hinders timely ACS therapies. In turn, this may complicate clinical risk assessment, with atypical presentation leading to 23.8% of ACS being misdiagnosed on admission; subjected to poorer use of evidence-based medication and higher adjusted in-hospital mortality.[29] It has been reported that the elderly have on average a 10% greater chance (than the young) of a change in ACS diagnosis on admission to that at the time of discharge from hospital.[10] Attending physicians, when faced with this uncertainty in diagnosis, may adopt a 'first do no harm' approach, offering more conservative management options until greater clarification when the results of targeted investigations, such as the cardiac Troponin, are available.[30]

The predicted risk of an ACS event is made in conjunction with age, on presenting findings, such as, ST-deviation, systolic blood pressure and heart rate. However, older patients have greater frequency of physiological impairment (frailty), psychological and cognitive impairment, physical disability and co-morbidity which enhance their age-related risk.[23] These are unlikely, however, to be considered and lower risk estimates may persuade healthcare professionals from adopting a more aggressive approach to the management of older patients.

Elderly patients with ACS are more likely to have additional co-morbidities than those of younger age, including renal impairment.[10] In addition, decreasing lean body weight[23] and varied drug metabolism in elderly patients (plus increasing potential for drug interaction with age) make correct dosing of medication difficult.[31] This leads to concern of greater harm over good, despite being higher risk ACS patients. Such concern has legitimacy, with 65% of patients older than 75 years receiving at least one excess dose of glycoprotein IIb/IIIa inhibitors and a higher risk of major bleeding with increasing numbers of antiplatelet and antithrombin drugs used.[32,33]

There is a paucity of evidence from RCTs to guide the management of elderly patients with ACS. To date, over 50% of trials concerning CHD have failed to enroll patients over the age of 75 years, and in total, this group represents only 9% of all trial patients enrolled; only 2% account for patients greater than 85 years of age.[23] There is a discrepancy between trial populations and the "real world" : trial patients accented into RCTs are often younger, male, and less frequently have renal impairment and heart failure.[23] Typically in trials, elderly patients less frequently have risk factors for CHD, less renal impairment, and better hemodynamics on presentation to hospital.[23] Given this, results from RCTs based on lower risk elderly ACS patients, who have less to gain from aggressive or invasive ACS therapies, may not accurately depict the true risk benefit ratio of treatment for real world, higher risk elderly patients with ACS.

Furthermore, a statement by the American Heart Association on ACS in the elderly reviewed many therapies by older age group presented in RCTs. Treatments, such as, clopidogrel or glycoprotein IIb/IIIa inhibitors showed varied relative benefits with increasing age, whereas, the use of heparins in older age lacked sufficient data. They also concluded there was a lack of evidence of benefit from PPCI over thrombolysis for patients older than 80 year of age with STEMI.[23,24]

4 Improving quality of ACS care in the older population

It has been suggested that improving the provision of evidence-based care in elderly with ACS offers the opportunity to improve overall outcomes.[34–36] Improved in-hospital mortality rates across all age groups, including the old (over 75 years old) and very old (85 years or older), were reported in a study from 2003 to 2010 of the Myocardial Ischemia National Audit Project registry of England and Wales.[10] Patients aged 85 years or older hospitalized with ACS had greater relative risk reductions for in-hospital mortality from 2003 to 2010 for both STEMI (30.1% to 19.4%; RR = 0.54, 95%CI: 0.38–0.75, $P < 0.001$) and NSTEMI (31.5% to 20.4%; RR = 0.56, 95%CI: 0.42–0.73, $P < 0.001$) compared with their younger counterparts (less than 55 years of age) with STEMI (2.0% to 1.5%; RR = 0.72, 95%CI: 0.39–1.25, $P = 0.24$) and NSTEMI (1.9% to 0.9%; RR = 0.89, 95%CI: 0.48–1.34, $P = 0.43$).

Improved outcomes also accompanied improved use of evidence-based therapies, including PPCI, in older ACS patients from 2003 to 2010.[10] This highlights the success of the National Service Framework for CHD in England and Wales from 2000 to 2010,[37] a national implementation plan to change delivery of care and encourage the use of contemporary evidence-based therapies. It also provides support to the notion that increasing use of evidence-based therapies in the elderly population with ACS is associated with improved clinical outcomes.

However, despite advances in the quality of ACS care from 2003 to 2010, age related inequalities are apparent.[10] For example, older ACS patients have been shown to have a higher incidence of previous myocardial infarction (less than 55 years of age: 21.2%, 85 years or older : 31.1%), but less often received previous revascularisation (less than 55 years: 9.1%, 85 years or older: 4.9%).[10] Patients aged 85 years or older hospitalized with STEMI were up to 75% less likely to receive either PPCI or thrombolysis than those less than 55 years of age (RR = 0.27, 95% CI: 0.25–0.28). Addi-

tionally, patients aged 85 years or older discharged with a diagnosis of ACS less frequently received aspirin, clopidogrel, ACEi, β-blockers and statins,[10] compared to those younger than 55 years. Addressing this age disadvantage by encouraging and implementing strategies nationally and internationally, to improve the delivery of evidence-based management to older ACS patients, may further improve care and patient centered outcomes.

5 Conclusions

Age related inequalities in patient care, to some extent, can be explained by the higher frequency of atypical and delayed presentations, and less diagnostic procedures such as ECG at presentation in the elderly, potentiating a delay in ACS diagnosis. Underestimation of mortality risk in the elderly due to limited consideration of physiological frailty, co-morbidity, cognitive/psychological impairment and physical disability, less specialist cardiology input and lack of randomised, controlled trials data to guide management in the elderly may further confound inequality of care.

The selection of elderly patients for specific therapies and medication regimens are unanswered. There is a growing need for RCT data to be more representative of the population and enroll those of greater age with co-morbidity. A lack of reporting of adverse events, such as renal impairment post coronary angiography, in the elderly further limit risk benefit decisions. Ultimately, improvements in the care of elderly patients with ACS are likely to lead to better outcomes as described by Gale *et al*.[30] However, the improvement in outcome is not infinite and will be limited by non-modifiable factors of age related risk.

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