Acute coronary syndrome management in older adults: guidelines, temporal changes and challenges

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Abstract

Advancing age is a risk factor for the development of coronary artery disease and is an important indicator of outcome after acute coronary syndrome. As the number of older adults increases, the burden of cardiovascular disease is set to grow particularly as older adults remain disadvantaged in the delivery of acute cardiac care. This article reviews the temporal changes in the provision of guideline recommended therapies for the management of acute coronary syndrome, discusses reasons for age-dependent inequalities in care and the challenges facing clinicians.

Keywords: acute coronary syndromes, older adults, temporal changes, inequalities, outcomes, older people

Background

Coronary artery disease (CAD) and acute coronary syndromes (ACS) are the leading cause of mortality in the UK, Europe and North America with consequent economic and social care implications [1, 2]. In response, organisations for setting standards for high-quality care such as the National Institute for Health and Care Excellence (NICE) have provided evidenced-based guidelines for the recognition and management of ACS. The spectrum of ACS includes ST segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI) and unstable angina (UA) [3–8]. Nationwide implementation of these guidelines has been associated with a 50% reduction in mortality from acute myocardial infarction (AMI) between 2002 and 2010 [2]. The importance of this is reflected in the changing age demographics of our society. In the UK, from 2003 to 2010, life expectancy increased from 76.5 to 78.1 years for males and 80.9–82.1 years for females. From 2000 to 2010, the prevalence of cardiovascular disease in people over 75 years of age increased from 30.8 to 35.5% [2]. Given age is an independent indicator of poor prognosis following ACS, these statistics are of concern [9]. Age as a prognostic marker is reflected in the majority of ACS risk scores, including the Evaluation of the Methods and Management of Acute Coronary Events [10] and the Global Registry of Acute Coronary Events (GRACE) [11]. The provision of evidence-based therapies is less frequent in this high-risk group [12].

Current guidelines

Guidelines for the management of older adults are the same as for their younger counterparts, with the proviso that treatments should be personalised. This includes an appreciation of functional status, co-morbidities, ischaemic and bleeding
risk as well as the physiological changes associated with ageing such as impaired renal function [4, 6]. Recommendations pertinent to older adults are derived from limited evidence from subset analyses of major trials and non-randomised retrospective analysis of registry data are summarised in Table 1. Of note, as ACS risk scores often classify older adults as high risk, this favours an early interventional strategy with prescription of appropriate secondary prevention medications.

**Table 1.** Table showing the current evidence of treatment for ACS in elderly patients

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombolysis therapy</td>
<td>Offers mortality benefit over no reperfusion up to the age of 85 years. This includes accounting for treatment-related deaths resulting from ICH, stroke, shock, and myocardial rupture [3, 51]</td>
</tr>
<tr>
<td>Primary PCI</td>
<td>Primary PCI offers a better risk–benefit ratio compared with thrombolytic therapy but more data are needed in over 80s [3, 51]</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Recommended for all elderly patients with ACS in the absence of contra-indications. Relative benefits are greater in elderly patients [9, 52]</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Considered for elderly patients with high-risk ACS particularly those undergoing PCI [5, 6, 9, 52]</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>Better outcome rates than clopidogrel and was not dependent on age with ≥75 years of age performing similar to &lt;75 years. There was no difference in major bleeding complications between the two groups [53]</td>
</tr>
<tr>
<td>Antithrombin therapy</td>
<td>Consider use in high-risk patients. However, there is a lack of age subgroup data on efficacy and safety from RCTs [6, 9]</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitors</td>
<td>Consider use in older subgroups at the time of intervention and where renal dysfunction has been excluded [6, 9]</td>
</tr>
<tr>
<td>Early cardiac catheterisation</td>
<td>Recommended as demonstrates improved short- and long-term outcomes. However evidence from RCTs is limited in the elderly population and must be balanced against higher bleeding risk. A lack of subgroup data in those &gt; 80 years [4, 6, 9]</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Shown to have greater benefits compared with younger population in prevention of subsequent AMI and death [6, 51, 52]</td>
</tr>
<tr>
<td>Angiotensin-converting-enzyme inhibitor</td>
<td>Shown to be beneficial, particularly in heart failure or reduced left ventricular function [51, 52]</td>
</tr>
<tr>
<td>Statins</td>
<td>Shown to have greater benefits compared with younger population in prevention of subsequent MI and death [3, 51, 52]</td>
</tr>
<tr>
<td>Cardiac rehabilitation</td>
<td>Shown to have comparable benefits compared with younger population in prevention of subsequent death [45, 46]</td>
</tr>
</tbody>
</table>

**Temporal changes in ACS management in older adults**

Registry data highlight temporal improvements in mortality from AMI that are age dependent [12, 13, 14, 15, 16, 17]. For example, data from the Myocardial Ischaemia National Audit Project (MINAP) showed reductions in in-hospital mortality in those over 85 years from 2003 to 2010 (STEMI: 30.1–19.4% and NSTEMI: 31.5–20.4%, respectively) [12]. Short term (30 days) data from MINAP has shown sustained improvements in mortality in those over 80 years with NSTEMI (18.9–15.0% from 2004 to 2009) [14]. A study from Quebec, using the Med-ECHO database, has shown 1-year mortality in those over 80 years of age with AMI declined between 1996–1999 and 2003–2006 (46.5 versus 40.9%, P < 0.001) [15].

These improvements are due to a combination of factors. Notably, there has been increased provision of early invasive intervention in patients over 80 years from 2004 to 2009 with higher rates of primary percutaneous coronary intervention (PCI) (2.0 versus 36.1%) and coronary angiography after AMI (11.5 versus 25.5%) [14]. Analysis of prescribing patterns has shown improvements in prescribing evidence-based therapies such as aspirin on admission (76 versus 86%) [12]. Data submitted to the National Institute for Cardiovascular Outcomes Research (NICOR) suggest increased crude 6-month mortality in centres in the lowest quartiles of delivery of coronary angiography (16.4% in quartile 1 versus 12.8% in quartile 4) and primary PCI (15.8% in quartile 1 versus 12.4% in quartile 4) [16]. There are temporal improvements in the prescription of secondary prevention medications. In those aged over 85 years, the rates of prescription of clopidogrel (28–89%), beta-blockers (49–56%) and statins (61–68%) on discharge have increased from 2003 to 2010 [12]. These improvements in provision and subsequent reductions in mortality have also been observed in North America [13, 15].

Data from the aforementioned registries demonstrate that this high-risk population benefit from early intervention and prescription of secondary prevention medications. This is corroborated by evidence from randomised controlled trials (RCTs) (Table 1). Despite these improvements older adults continue to have lower rates of survival [17] are less likely to receive guideline recommended care particularly with regard to interventional therapies [12] and the prescription of dual anti-platelet therapy [17].

**Identification of ACS in older adults**

In older adults, the diagnosis of ACS is often challenging. In one study, 8.4% of patients with ACS presented without chest pain of which 43.3% were over 75 years of age compared with 29.4% of patients <65 years of age [20]. Older adults commonly present with autonomic symptoms including dyspnoea (49.3%), diaphoresis (26.2%), nausea and vomiting (24.3%), but also with pre-syncpe and syncope...
(19.1%) [20]. Chest pain is present in ~40% of those over 85 compared with nearly 80% in those under 65 [9]. Consequently, there is a reduced probability of ACS being diagnosed and an increased incidence of acute decompensation and in-hospital mortality [20].

Delays to the provision and reporting of the initial ECG may delay diagnosis [9]. Notably, more than two in five of ACS patients over 85 years of age do not have diagnostic ECG changes compared with a quarter of those under the age of 65 years [9]. These factors may cloud the clinical picture and prevent timely diagnosis of ACS.

In the case of STEMI, the myocardial infarction may be more evolved, with greater loss of myocardium and an increase in acute complications.

**Risk stratification**

National and international guidelines recommend early risk stratification using validated scoring systems, such as the GRACE risk score to identify patients appropriate for an invasive strategy [3–8]. Age is a component of risk stratification as in-hospital mortality is significantly higher in older adults. In 2010 in-hospital mortality for NSTEMI in those over 85 years of age was 20.4% compared with 0.9% in those <55 years. [12]. Objective algorithms for risk-scoring are often not adopted as often clinicians subjectively assess an individual’s risk [21]. Evidence from the Canadian ACS-2 registry [22] suggests that risk is often underestimated; this inevitably influences subsequent management as those deemed at highest risk more frequently undergo intervention. This study found that older adults were paradoxically assigned to an inappropriately low-risk group. Risk scores have their limitations including a lack of bedside convenience and some data only being available following an angiogram or biochemical test [23]. As age is incorporated into most risk score algorithms older adults will be scored as higher risk-based on their age alone. Risk scores do not take into account factors such as frailty associated with ageing.

**Frailty and co-morbidities and their influences on referral for revascularisation**

The presence of frailty is associated with reduction in cardiac catheterisation [24] and higher rates of institutional discharge [28]. Data from MINAP suggest that patients aged over 80 years have higher proportions of diabetes mellitus (16.7 versus 13.3%), heart failure (11.1 versus 1.6%) and renal failure (7.8 versus 1.7%) compared with those under 65 [12]. There is a greater prevalence of anaemia, cerebrovascular disease and dementia [9, 29]. Presence of conditions such as anaemia, especially when causation is unclear, limits the prescription of dual anti-platelet therapy and may delay invasive interventions. The presence of dementia is associated with 27% less chance of receiving an interventional strategy [adjusted odds ratio (OR) = 0.73; 95% CI 0.63–0.83] and 22% less chance of being prescribed guideline-recommended medications (adjusted OR = 0.78; 95% CI 0.68–0.89) [30].

Co-morbidity raises issues with polypharmacy in patients who have age-related physiological changes in drug metabolism and renal function. Beta-blockers may worsen heart failure in those with acute cardiac failure, mediate bronchoconstriction in chronic obstructive pulmonary disease and increase claudication in peripheral vascular disease [19]. The extent of adverse drug reactions (ADRs) is associated with the number of drugs taken. An increase in ADR from 13% in patients taking two medications to 82% in patients taking 7 or more has been reported [31]. Importantly, older adults more often have contra-indications for therapies. In the GUSTO-1 trial, nearly 10% of elderly patients had absolute contra-indications to thrombolysis [32]. However, in the era of 24 h primary PCI, these therapies are less likely to be utilised (Table 1). This is especially relevant in older adults where intra-cerebral haemorrhage is a significant risk (0.4% in patients aged <65 years to 2.13% in patients aged ≥75 years) [33].

**Application of evidence from trial populations in older adults**

In 2001, participants over 75 years made up only 9% of the study population in RCTs with ACS [34]. One review of 593 RCTs found that 40% of trials excluded people based on their age between 1991 and 2000 [34]. The situation is improving with recent data reporting that the proportion has risen to nearly 14% [35]. In the recent PCI RCTs SYNTAX [36] and LEADERS [37], there was no age exclusion criterion. Generalisation of RCT data to real-world populations is difficult due to the large differences in patient characteristics between these cohorts. Data from the CRUSADE study, which compared trial populations to disease registries, suggested that patients in trials were younger, had lower rates of heart failure (13.2 versus 19.0%), renal insufficiency (8.5 versus 13.9%) and stroke (8.1 versus 11.1%) [38]. Elderly patients in trials also less frequently have risk factors for CHD, fewer co-morbidities, better renal function and haemodynamics than real-world populations [9].

The lack of subgroup data and safety and efficacy are highlighted in Table 1. Concern over the increased risk of major bleeding with PCI [39] and the use of glycoprotein IIb/IIIa inhibitors is legitimate [9]. Bleeding as a complication of PCI is associated with an increase in morbidity and mortality [40]. The use of verified risk assessment scores for bleeding, such as CRUSADE, which do not include age may enable more objective assessment of the risk of harm associated with a procedure [41]. Careful consideration should be given to dosing of anti-thrombotics as an increased incidence of renal failure and low body weight can lead to toxicity. Clinically, this is important as excess doses of low-molecular-weight heparin (OR, 1.39; 95% CI 1.11–1.74) and glycoprotein IIb/IIIa inhibitors (OR, 1.36; 95% CI 1.10–1.68) had a higher risk of major bleeding [42].
Access to care pathways

Patients over 80 years hospitalised with ACS are less frequently admitted directly to coronary care units (39.1 versus 64%) or under the care of a cardiologist (30.1 versus 51.1%) compared with those <65 years of age [17]. The reasons for this are unclear though it highlights a risk-treatment paradox whereby higher risk patients are less likely to receive evidence-based care [43].

Post-ACS care provision

There is a longer length of stay following ACS (8 days for those over 80 years versus 5 days for those <65 years) [17] and cardiac surgery. One study of 12,017 patients following coronary artery bypass graft (CABG) surgery in North America demonstrated that those over 75 years of age had 27.3% longer length of stay compared with those <75 years (11.2 ± 9.9 versus 8.8 ± 8.1 days; P < 0.0001) with an 11% increase in cost [44]. Evidence from studies in frail individuals demonstrates longer hospital stays and increased rates of discharge to institutional care [27, 28]. These factors will have significant implications for bed occupancy and health economics.

Utilisation of cardiac rehabilitation programmes in older adults is low. Only 13.9% of AMI patients and 31% of CABG patients aged over 65 years participate in a cardiac rehabilitation programme and these numbers are worse for older individuals [45]. Crude rates of cardiac rehabilitation in men over 85 years are only 4.6% compared with 26.6% in those aged between 65 and 74 years [45]. Use of cardiac rehabilitation is associated with 21–34% reductions in mortality rates, which are comparable with younger populations, [46] as well as improvements in cardiac risk factors, exercise capacity and quality-of-life [47]. The reasons for low uptake of cardiac rehabilitation are multi-factorial and complex. However, the strength of the primary physician’s recommendation for participation has been identified as a powerful predictor of entry into programmes [48] which suggests that there is scope for improvement.

Discussion

Management of ACS in older adults remains a clinical challenge despite guidelines outlining care pathways. The ageing population means the burden of ACS will increase particularly in older adults. Trial evidence (Table 1) and epidemiological data indicate the benefit of an early evidence-based approach. Temporal improvements in the delivery of ACS care in older adults have been documented but disparities continue to exist, which indicates that there is still scope to improve outcomes.

The impact of the physiology of ageing on an individual may be difficult to assess quickly in an acute setting such as an ACS. The clinical relevance of altered drug metabolism is uncertain, especially between individuals. Difficulties with immediate pharmacotherapy decisions and perhaps a reluctance of physicians to prescribe medications with potential adverse effects are an area of concern. There may be a reluctance to prescribe some medications such as beta-blockers due to concerns over efficacy and the potential for worsening cardiac output [19]. The controlled environment of a hospital ward should allow these medications to be administered and any adverse effects promptly treated. The degree of polypharmacy and renal handling issues could be addressed by early involvement of pharmacists and elderly care physicians to rationalize medications and ensure correct dosing regimens. This strategy is particularly important in the management of ACS as providing a guideline-based approach may potentially contribute to polypharmacy. Therefore, rationalising medications, particularly stopping drugs with limited prognostic benefit, could improve adherence to guidelines. Some classes of drugs, for example, statins, may also be indicated for several conditions given the prevalence of other vascular disease in individuals with CAD. There is evidence that currently these are under prescribed in the elderly. [12]. Medications such as ACE-inhibitors could be withheld until after intervention in order to minimise the risk of contrast nephropathy. There is a need to carefully dose drugs such as low-molecular-weight heparins and glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors to minimise bleeding risk.

Recognition of ACS has also been highlighted as a significant area of concern. The prevalence of atypical presentation and non-diagnostic ECGs are non-modifiable and will lead to delays in diagnosis and treatment. Therefore, clinicians need a high index of suspicion of ACS and refer early for specialist opinion. This will enable timely provision of guideline-based therapies. However, ascertaining the relevance of raised cardiac biomarkers in elderly individuals with the presence of a concurrent acute illness and no other features of AMI remains challenging.

The burden of co-morbidities also presents difficulties in the provision of evidence-based care. Higher rates of anaemia and renal disease need consideration before exposure to a procedure with potential side-effects of bleeding and further renal impairment. This may lead to further delay in appropriate treatment. Vascular access sites should be carefully considered as part of the risk assessment before considering an invasive strategy as the elderly are more likely to have calcified and tortuous great vessel anatomy with increased bleeding risk. The extent of intervention may also be an issue due to the increased prevalence of multi-vessel and complex disease that is evident following angiography [39]. Clinicians may therefore adopt a ‘first, do no harm’ approach. Procedural consent may be more difficult with higher rates of dementia, hearing and visual impairment [9].

These concerns are justified but the epidemiological data show us improved outcomes in older adults despite the greater burden of co-morbidities [12]. Perhaps greater utilisation of risk scores can aid this decision process. We know that risk scores are currently poorly implemented in clinical practice and that older adults are often subjectively assigned to lower risk groups. This potentially has huge implications on subsequent management and means they are less likely to
receive interventional therapies. Further evaluation is needed to validate frailty risk scores, which assess different factors to traditional risk scoring systems, to determine whether they help identify which of this high-risk group have the most to gain from an interventional approach. Using verified bleeding scores such as CRUSADE can provide objective data of potential harm to enable clinicians to make balanced objective risk–benefit decisions. Clearly, an interventional treatment strategy is not in every patient’s interests and therefore use of risk scoring systems may help identify these individuals. Its important to take into account patient preferences and objective data can aid both clinicians and patients during the consent process.

There is a need for RCTs to more accurately reflect the population and not only consider procedural efficacy and safety but the longer term effectiveness of revascularisation in older adults. Numerous previous authors have suggested this solution and there has been minimal improvement in the proportion of older adults in trial populations. The large costs involved in setting up clinical trials and a lack of understanding of the heterogeneity of the ageing process means this is unlikely to change in the future. However, the looming explosion in the elderly population mean gathering evidence for ACS management is vital. Alternative approaches such as those employed in trial-registries like the Thrombus Aspiration in STEMI in Scandinavia (TASTE) trial based on the Swedish angiography and angioplasty registry (SCAAR) platform [49] may be beneficial.

Access to specialist cardiologist facilities remains an area of concern. Elderly patients who are not under the care of a specialist have delays to diagnosis and the provision of guideline recommended therapy, and less access to interventional strategies [43]. The reasons for this are not clear but may include a desire by the admitting physician to preferentially treat those who are younger because this group is perceived to have more to lose in the longer term. Longer length of stays for elderly patients will become a larger concern in the future and may have significant impacts on availability of coronary care beds and health economics. Development of an elderly cardiac team, encompassing cardiologists, elderly care physicians and rehabilitation teams could ensure those with the greatest potential benefit have access to interventional services as well as reducing hospital stays.

Further research in to post-AMI management strategies in elderly patients could help improve outcomes in conjunction with greater utilisation of cardiac rehabilitation. Longer term the development of an ACS guideline for older adults, similar to NICE hip fracture guidelines [50], could enable a more co-ordinated approach to both delivering immediate ACS care and ongoing post AMI management.

Conclusion

The ageing population in Western countries means the burden of ACS will continue to increase in the forthcoming years. This will have significant implications on health economics and social care. Management of ACS in older adults remains complex due to a lack of randomised controlled trial evidence, poor understanding of the ageing process on the cardiovascular system and difficulties with identification of ACS.

Recent studies have demonstrated temporal improvements in inequalities of care provision in ACS patients although substantial age-dependent inequalities persist. Enhanced utilisation of risk scoring systems can aid decision-making and enable greater tailoring of therapies to individuals. A greater understanding of the impact of frailty on outcomes and management is needed in conjunction with developing multi-specialty teams to co-ordinate early application of appropriate guideline-based therapies.

Key points

- Advancing age is a significant risk factor for adverse outcomes following ACSs.
- Temporal improvements in provision of guideline-based management have been observed in older adults.
- Older adults remain disadvantaged in the current provision of evidence-based care.
- Management of ACS in the elderly is hindered by a lack of high level evidence.
- Risk stratification and early application of appropriate management strategies would likely improve outcomes.

Conflicts of interest

None declared.

References

The very long list of references supporting this review has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on Supplementary data in Age and Ageing online, Appendix S1.


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