Managing myocardial infarction in the elderly: time to bury inappropriate concerns instead

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This editorial refers to 'Changes in management of elderly patients with myocardial infarction', by F. Schiele et al., on page 987

'Age is not a particularly interesting subject. Anyone can get old. All you have to do is live long enough'
Groucho Marx (1890–1977)

‘Of all the self-fulfilling prophecies in our culture, the assumption that aging means decline and poor health is probably the deadliest’
Marilyn Ferguson, The Aquarian Conspiracy, 1980

An ageing population, the prevalence of cardiovascular disease as a major cause of morbidity and mortality, and the development of potent therapies with potential life-threatening side effects present challenges for patient care that are increasingly likely to require serious consideration in coming years. In general, cardiovascular mortality and morbidity have fallen as therapeutic advances have been implemented, especially in the management of acute coronary syndromes (ACS)—here potent anti-platelet/anti-thrombotic agents have improved non-ST-elevation myocardial infarction (NSTEMI) outcomes, and in ST-elevation myocardial infarction (STEMI) management, the use of thrombolytic plus adjunctive pharmacotherapy and the uptake of primary percutaneous coronary angioplasty (P-PCI), also with its requirement for potent adjunctive anti-thrombotic/anti-platelet regimens, have each, in turn, reduced morbidity and mortality. It is the full application of such therapeutic strategies in elderly patients that raises general concerns and present issues about optimal care that need addressing.

The number of older adults has risen >3-fold since 1950, from ~130 million to 419 million in 2000, with the elderly share of the population increasing from 4 to 7% during that period. The population in Europe is ageing rapidly. Europe has 19 of the world’s 20 countries with the largest percentage of elderly people. In Italy >19% of the population are elderly, a figure expected to reach 28% by 2030. An important perspective on the problem and how this relates to cardiovascular disease is outlined in the ‘Cardiovascular Diseases in Europe Euro Heart Survey 2006’ edited by Wilma Scholte et al. This group reported that 13.7% of the European population is aged >65 years—twice the world level. The current percentage aged >65 years is expected to double to ~30% by 2050. For every 100 persons aged 25–64 years in 2050, there will be 57 who will be >65 years (currently 28 per 100). In the USA, the Census Bureau (2004) projects that in 25 years this proportion will exceed 20%—within the next 50 years one citizen in five will be 65 or older—by 2050 one American in 20 will be 85 years old or older, compared with one in 100 today. Both the American population and the population of the world are adding oldest-old members at a much faster rate than any other age group.

Each year cardiovascular disease causes >4.3 million deaths in Europe. With increasing age, the prevalence of cardiovascular disease and death associated with it increases steeply. In total, ~40% of deaths are caused by cardiovascular diseases, but this may reach >50% in the elderly. Despite positive developments in prevention and treatment that for the general population have reduced mortality and morbidity, and led to improvements in quality of life, the total burden of cardiovascular disease will remain high due to the population ageing.

These considerations make the elderly legitimate targets for the new developments in cardiovascular medicine; an important task for the coming decades will be to provide satisfactory levels of well-being to elderly patients, including providing available optimal cutting-edge care, if appropriate, in qualitative and quantitative terms. This will need to be in the face of concerns about the medical (safety) applicability of new devices and pharmacotherapy in this group, not to mention the pressures of limited financial resources. The supposed direct clear modern incisive application of evidence-based medicine as developed through Guidelines, with delivery of proven new management strategies, often seems to evaporate into a vague patchy, ad hoc approach when elderly patients present with acute cardiovascular disease.
Furthermore, managing elderly patients is about more than mortality. Quality of life issues are important, with more elderly patients wishing to be self-reliant, to be involved in social activities, and disinclined to be included in their children’s households or in elderly institutions.

It is important to explore the reasons for the failure always to apply modern management strategies to the elderly. Clearly there are sometimes good reasons and sometimes poor or inappropriate reasons. For example, despite the development of National, Professional Society and International Guidelines for the management of acute cardiovascular disease and demonstration that adherence to guidelines generally improves outcomes, in many hospitals such Guidelines are only partially implemented, irrespective of age group. Even if applied, most Guidelines allude to the elderly only as a section or subsection within them—there appear to be no specific Guidelines solely applicable to the elderly. The importance of clear guidance pertaining to the elderly is important since if there is available evidence (and therein lies another problem, since there are less evidence-based data for elderly populations), and it is appropriately applied, the effects achieved in the elderly can be as convincing as in the young in terms of mortality, morbidity, and quality of life. Even where there are clear data for benefit in the elderly patients, undertreatment is common in this group, perhaps consequent on concerns regarding side effects of polypharmacy and the impact of co-morbidities. Focusing on the development of clear Guidelines for the management of acute cardiovascular disease specifically in the elderly will have other potential beneficial spin-offs. Elderly patients present later and will delay seeking medical help when they experience the first symptoms of myocardial infarction, contributing to higher mortality and morbidity. Clear algorithmic management strategies developed by committed, convinced cardiologists should lead to improvements in patient education, increased compliance, and earlier recognition of complications and side effects of medication.

Schiele and colleagues have observed the changes over time in the management of elderly patients with myocardial infarction. They looked at two periods, the first a 6-month and the second a 12-month period, 5 years apart and compared the demographics and in-hospital treatment between the two periods with an endpoint comparison of mortality at 1 month during each of the study periods. Such observational comparisons can be notoriously difficult to interpret—is any difference in outcome explicable only in terms of changes in treatment? Could it be that the groups are different in other ways and that it is these differences that influence outcome? Have approaches to such patients changed over the time period? Has there been overuse of a propensity analysis, which is sometimes seen as the solution for smoothing out the differences so that only the factor you are interested in (in this case change in therapy) can be convincingly shown as the cause of change? Propensity analysis, whilst a useful statistical tool, is not the statistical panacea that some like to believe it is. In particular, the groups may be so different that any statistical correction cannot be used to adjust for differences. Understanding the importance of the C-statistic value may provide insight into whether, if too low, important variables are missing in the model. While the C-statistic here was quite low at 0.67, it would appear that all the important variables have been included [including the components of the GRACE (Global Registry of Acute Coronary Events) score] and thus the cohorts probably were not significantly dissimilar other than the second cohort being a higher risk group. The conclusion therefore that the significantly lower 1-month mortality in the second cohort (7.1%) compared with that (13.6%) in the first cohort was indeed due to change in intensity of treatment, probably holds up (and that this was driven mostly by change in mortality in the STEMI group). Of particular interest is the change from thrombolysis to P-PCI over this period and the benefits associated with increase in use of glycoprotein (GP) IIb/IIIa despite the bleeding risks in this group. Although GP IIb/IIIa is being replaced in many centres with a strategy of optimal doses of clopidogrel plus direct thrombin inhibitors, the data on GP IIb/IIIa in this study emphasize the fact that with the use of evidence-based therapies, even those that have potential side effects, the benefit/risk balance may still apply to elderly patients. The message from the authors that elderly patients benefit from evidence-based therapies is an important, albeit not new, one. Although elderly patients do worse in terms of outcomes compared with younger patients, even following the use of evidence-based strategies (co-morbidities such as risks of cerebrovascular accident, bleeding, low body weight, fragile vascular system), they still do better if treated with evidence-based Guideline-mandated therapies.

Age itself is a risk factor—in one paper the risk of death of patients between 75 and 84 years [odds ratio (OR) 4.15, 95% confidence interval (CI) 1.70–10.15] and between 85 and 94 years (OR 4.68, 95% CI:1.62–13.52) was higher than in the 34–64 years age group, independently of any patient characteristic. However, in the Fibrinolytic Therapy Trialists Collaborative group study, for example, benefit from lysis was observed among patients presenting with ST elevation or bundle-branch block (BBB)—irrespective of age, and Stenestrand reported fibrinolytic therapy in patients with STEMI who are ≥75 years as being associated with a reduction in the composite of mortality and cerebral bleedings after 1 year. Even in the original thrombolytic ISIS-2 trial followed-up for up to 4 years, those who were >70 years did better with lytic treatment than not, although not as well as the younger cohort—a review of all reperfusion data led Boersma to state ‘the absolute number of deaths avoided by reperfusion therapy appears to be greatest in those groups with a high mortality risk without therapy’. We found in the REACT trial that those elderly patients receiving rescue PCI did better than the same age group who received conservative management although again they did not do as well as the younger patients receiving R-PCI, and as in many such studies the numbers dwindle in the outreaches of age. In particular, the elderly appear to do better with P-PCI than those of the same age who received thrombolysis.

Despite these beneficial outcomes in the elderly, the GRACE registry report looking at the impact age on management of ACS indicated that there was an increase in delay in the elderly in seeking medical attention and that evidence-based medications, including aspirin, β-blockers, and statins, were less often prescribed in elderly patients. Rates of coronary angiography and PCI use decreased with advancing age. At the same time, adverse outcomes, including stroke, cardiogenic shock, and
in-hospital mortality, increased with age, which perhaps supports an inappropriate bias towards undertaking coronary interventions in younger and healthier patients.\(^1\)\(^1\)

So why is there a reluctance to deliver proven and mandated treatments to the elderly when over the past decade the management of patients with ACS has evolved so rapidly with the development of new therapies and management strategies which have led to improved survival and improvements in life expectancy? Such advances have primarily been seen in those <65 years and in men, yet, while the elderly are a subgroup known to be at high risk, less use of cardiac medications and invasive care, even among those elderly individuals likely to benefit, has not been optimal. One problem is the limited randomized clinical trial data to guide acute care in elderly patients, with many trials having cut-offs for age recruitment—the current approach to enrolling the elderly in trials limits the applicability of available evidence, which in turn results in there being no Guidelines available specifically directed towards the elderly (>65 years, >70 years, >75 years, >80 years; what is elderly?). True there are position statements such as that from the American Heart Association (AHA; in association with the Society of Geriatric Cardiology),\(^2\)\(^3\) but maybe there is a serious need for the publication of formal Guidelines directly applicable only to the elderly. Highlighting that the elderly with NSTE ACS may have atypical presentations, with absence of chest pain, and non-diagnostic ECGs, will raise the profile and lead hopefully to physicians having a high index of suspicion and maybe helping to shorten presentation times. In addition to higher short-term and long-term death rates, older NSTE ACS populations experience more chronic heart failure (CHF) and bleeding complications. Given the common occurrence of renal and other factors that can alter drug metabolism, attention to therapeutic dosing in such Guidelines is crucial. Thus any Guidelines should include evidence-based data (such as there are) on adjusted dosing of the agents about which there might be justifiable concerns. Sometimes there is available advice on dose adjustment, but mostly this is weight adjusted (as with GPIIb/IIIa, unfractionated and low molecular weight heparin), sometimes there is none (as with aspirin and/or clopidogrel), and sometimes there are no data on the excess risk/less benefit ratio in the elderly. This all leads to lingering uncertainty about benefit and risk of newer therapies and strategies in those with advanced age. Providing Guidelines specifically aimed at the elderly is important since for gains in quality life-years after ACS to continue, survival from acute heart disease will need also to extend to the elderly and very elderly population. Understanding how treatments are effective in realizing patient-centred outcomes in this subgroup is important. Planned trials in the elderly alone with careful risk/benefit analysis leading to Guidelines in acute cardiac care specifically for the elderly must be the way forward. Although some recent trials describe treatment effects in the older patient, others have an age inclusion cut-off. There should be trials that specifically enrol elderly subjects in direct relationship to the number in those being treated in the general population, with the risk/benefit ratio being emphasized, and all reporting should be consistent, and include the impact of the proposed therapy on measures of quality of life.

The study by Schiele and colleagues\(^4\) should remind us that although making therapeutic decisions following acute cardiovascular presentation in the elderly can be fraught with anxiety about appropriateness and risk, and understandably not easy, we should apply the evidence base that is available and push for more elderly-based trials and improved Guidelines to ensure we are not denying this increasing patient population optimal care.

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References