Editorial

STEMI care in the elderly: Does under-treatment reflect appropriate clinical judgment or therapeutic nihilism?

Cardiovascular disease burden rises with increasing age and it remains the leading cause of morbidity and mortality in the elderly. In the United States (U.S.), roughly one-third of deaths in the elderly each year can be attributed to acute coronary syndromes (ACS).[1] However, clinical trial populations have traditionally been fraught with the problem of inadequate depiction of the 'real-world' demographics of ACS patients. The proportional representation of elderly patients in ACS clinical trials is much lower (∼10%) than that seen in everyday clinical practice, where around 35% of ACS patients are aged ≥75 years.[2] Since data from trials exclusively enrolling elderly patients are scarce, the current management of elderly patients with ACS is essentially dictated by subgroup analyses from major ACS trials. This evidence does demonstrate the effectiveness of both timely coronary reperfusion and secondary prevention medications (such as beta-blockers, statins, and angiotensin-converting enzyme (ACE) inhibitors/aldosterone II receptor blockers (ARBs)) even in the oldest group of patients.[3] However, multiple studies have shown that the elderly are much less likely than the younger patients to receive these ACS therapies.[4] Moreover, community elderly patients with ACS are sicker and more likely to have hypertension, prior stroke, acute heart failure, cardiogenic shock, and atrioventricular block (AVB) than trial patients. Therefore, there is a dire need of real-world clinical data on the presenting characteristics, receipt of treatment strategies, and outcomes in the elderly patients with ACS, as well as temporal changes in these parameters.

In this issue of the *Indian Heart Journal*, Jomaa et al.[5] examine the differences in baseline clinical characteristics, rates of reperfusion therapy, and in-hospital outcomes in elderly patients aged ≥75 years ($n = 211$; 15%) vs. those aged <75 years ($n = 1192$; 85%) in a cohort of 1403 patients presenting with ST-elevation myocardial infarction (STEMI) to a Tunisian University hospital over a 16-year period from 1998 to 2013. Elderly patients were less likely to be women and more likely to be hypertensive and anemic. The prevalence of smoking and obesity was lower in the elderly group. Fibrinolytic therapy (22.3% vs. 36.6%, $p < 0.001$) and primary percutaneous coronary intervention (pPCI; 24.2% vs. 28.8%, $p = 0.17$) were less frequently utilized, whereas conservative medical therapy

was more common in the elderly (43.1% vs. 28.9%, $p < 0.001$). Interestingly, there were no statistically significant differences in the time from symptom onset to reperfusion (either by thrombolysis or pPCI) in elderly vs. younger STEMI patients. As would be expected, complications such as heart failure and renal failure on admission, new onset atrial fibrillation, AVB, cardiogenic shock, and use of inotropes were more common in the elderly. Also, in-hospital mortality in the elderly was almost two-fold in comparison to the younger cohort (14.2% vs. 8.1%, $p = 0.005$). On multivariate analysis, heart failure on-admission, renal failure on-admission, and use of inotropic therapy were found to be independent predictors of in-hospital mortality. The authors also investigated the temporal trends in use of fibrinolytic therapy and pPCI as well as in-hospital mortality in both the elderly and younger age groups. Overall, although the use of both reperfusion strategies increased over the study period in both age groups, it remained lower in the elderly throughout. Intriguingly, there was a substantial increase in crude in-hospital mortality in both younger and elderly patients with STEMI over the study years, but the authors did not perform univariate or multivariate analysis to study the statistical significance of this trend.

There are several important points to consider while interpreting this study's findings. First, as pointed out by the authors themselves, their study population represents a largely urban cohort of patients with relatively westernized lifestyles and with ready access to modern STEMI systems of care, including trained emergency medical services (EMS) and pPCI facilities. Therefore, these results cannot be generalized to the broader Tunisian or North African populations, where a significant section of the population is still predominantly rural. This assumption is reinforced by this study's finding of no significant differences in the time from symptom onset to reperfusion in elderly vs. younger patients, whereas studies even in the U.S. setting have shown older age to be a predictor of longer pre-hospital delays.[3] Moreover, none of the patients in the current study were transfers from primary or secondary level of care healthcare facilities and all patients were brought directly to the emergency department of the University hospital by EMS services with a confirmed electrocardiographic (ECG) diagnosis of STEMI. It is well known that initial

presentation to non-STEMI centers without fibrinolytic and pPCI capabilities is associated with reperfusion delays due to both delayed recognition of STEMI and then the time needed for inter-hospital transfer, leading to worse short- and long-term outcomes. It is probable that the majority of the North African patients do not have access to these organized systems of care and indeed have much worse outcomes than that reported in this study.

The proportion of elderly STEMI patients (15%) in this study was lower than that what has been observed in the Western literature. Large multi-center U.S. ACS registries, such as the Global Registry of Acute Coronary Events (GRACE) and National Registry of Myocardial Infarction (NRMI), have reported the prevalence of elderly patients aged over 75 years to be around 30% in contemporary STEMI cohorts.[3] Whether the demographics of STEMI patients is different between Tunisian and the Western populations in general, or the lower proportion of elderly patients in this study represents some sort of a selection bias, will need to be established by future investigations.

The under-utilization of reperfusion in the elderly patients when compared with younger patients is consistent with results from several U.S. studies.[6] The current U.S. STEMI guidelines recommend treatment with reperfusion for patients presenting within 12 h of symptom onset in the absence of contraindications.[7] However, the proportion of STEMI patients eligible for reperfusion therapy decreases with age. Common reasons for elderly being ineligible for reperfusion therapy with fibrinolysis or pPCI include delayed presentation several hours after symptom onset, abnormal ECG at baseline, atypical ECG findings, and frequent absence of chest pain as a presenting symptom leading to a diminished suspicion for STEMI at the point of initial medical contact. Also, elderly are more likely to have both absolute (e.g. uncontrolled hypertension, recent stroke, history of intracranial hemorrhage, etc.) and relative (e.g. prior stroke, dementia, chronic anticoagulation) contraindications to fibrinolytic therapy. Moreover, findings from the GRACE registry show that an age ≥75 years is an independent predictor of failure to receive reperfusion therapy even in eligible patients.[8] Coexisting age-related frailty, high prevalence of comorbid conditions, frequent cognitive impairment, and patient preference are some of the reasons that potentially contribute to lower reperfusion rates in the reperfusion-eligible elderly patients.[3] Additionally, there is often the factor of "ageism", i.e. physician perception of lack of benefit from the use of an aggressive approach to treat STEMI in elderly patients, given the overall poor short- and long-term outcomes irrespective of the treatment strategy. Whether this represents reasoned clinical judgment or there is an element of therapeutic nihilism to this approach, remains a frequent matter of medical debate. Results from the British Myocardial Infarction National Audit Project (MINAP) show that the elderly are less likely to be even under the care of a cardiologist during their ACS hospitalization.[4] This, combined with the findings that older ACS patients are also less likely to receive proven medical therapies such as aspirin, beta-blockers, statins, ACE inhibitors/ARBs both during hospital admission and at discharge, does suggest that there is a component of nihilism to this practice of under-treatment in the elderly.[3]

The optimal modality of reperfusion for STEMI in the elderly is another conundrum. General consensus agrees that eligible older STEMI patients who receive reperfusion have more favorable outcomes than those who do not; limited data available in this population suggest that PCI may be more favorable over fibrinolytic therapy, especially among patients presenting more than 3–6 h after symptom onset, which is often the case in elderly patients. The major benefit of PCI over fibrinolysis appears to be from reductions in recurrent MIs and need for target-vessel revascularization with mortality benefits being more modest.[3] In the current study, 24.2% and 22.3% of the elderly patients over the age of 75 years with STEMI received reperfusion with fibrinolysis and pPCI, respectively. These rates are still much lower than contemporary reperfusion rates in the Western cohorts of elderly STEMI patients, where the reperfusion rates are in the 50–60% range (especially considering that this study's population does represent a somewhat selected cohort of patients presenting directly to a tertiary care teaching facility).[3,4] A surprising finding of the current study is the time trend in use of reperfusion. From 1998–2001 to 2006–2009, consistent with worldwide trends, use of thrombolysis decreased and pPCI increased in both younger and older patients. However, from 2006–2009 to 2010–2013, there was a prominent increase in thrombolysis rates accompanied with a decline in pPCI rates in both younger and older patients. Whether this trend was driven by a change in hospital practices or some other factors, has not been adequately discussed by the authors.

Consistent with results from the Western literature, in-hospital mortality among elderly with STEMI was almost two-fold higher than in the younger patients. Mortality rates with STEMI are known to increase with increasing age mainly due to more frequent occurrence of mechanical and electrical complications, such as heart failure, cardiogenic shock, high-degree AVB, and malignant ventricular arrhythmias.[3] The in-hospital mortality (14.2%) in this study though is actually quite comparable to that reported in contemporary Western reports.[9] The surprising finding here again is the temporal trend in in-hospital mortality. There was a noticeable increase in in-hospital mortality from 4.7% to 9.8% in the younger group and from 8.9% to 13% in the elderly from the early to late study years. This is in stark contrast to the Western literature where multiple studies have demonstrated a steady decline in in-hospital mortality after STEMI over the past couple of decades, especially among the elderly population.[9,10] The author's explanation of this finding being due to differences in pPCI programs between Western countries and Tunisia is not convincing since their data come from a single tertiary-care center and it is unlikely that there were major system-based changes within the institution over the study period. It would have been useful if the authors further explored the reasons behind this puzzling trend. Whether this was due to an increase in prevalence of comorbidities among STEMI patients over the study years? Were there changes in time to reperfusion over the years?

Lastly, the independent predictors of in-hospital mortality as defined in this study might not be all-inclusive. Though it is undeniable that acute heart failure, acute renal failure, and the need for inotropy predict mortality in STEMI patients, it is perplexing that well-known positive (thrombolysis, pPCI) and negative (female sex, diabetes, atrial fibrillation, AVB, reperfusion delays, cardiogenic shock) prognostic factors did not predict in-hospital mortality in this cohort of elderly patients

with STEMI. Is it tenable to say that cardiogenic shock does not predict mortality in elderly patients with STEMI? Or that thrombolysis and pPCI are not associated with a mortality benefit? The likely reason for this is the relative low sample size ($n = 211$) of the elderly STEMI population and therefore, inadequate power to accurately identify all the independent predictors of in-hospital mortality.

Despite these potential shortcomings, the investigators should be commended for conducting this important study. The findings of this study add greatly to our knowledge about the practice patterns in management and outcomes of STEMI in the elderly in the North African continent, from where published data in the English literature are extremely limited. Since randomized trials solely enrolling elderly patients with STEMI are unlikely – given the ethical considerations in randomizing elderly contemporary STEMI patients to reperfusion vs. conservative management – registry analyses, such as this, are important to further our understanding of ACS management practices in this vulnerable population.

Conflicts of interest

The author has none to declare.

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