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EDITORIAL COMMENT

Contemporary Management of Cardiogenic Shock

Age Is Opportunity*

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"How far the gulf stream of our youth may flow into the arctic regions of our lives. For age is opportunity no less than youth itself, though in another dress. And as the evening twilight fades away, the sky is filled with stars, invisible by day."

—Henry Wadsworth Longfellow (1)

The ability to select appropriate older patients for invasive management is one of the most important challenges for our healthcare system. Over 40% of patients with cardiogenic shock (CS), the most common cause of death after acute myocardial infarction (MI), are over age 75 years (2–4). They often have poor organ reserve and cannot withstand the hemodynamic stresses of shock, leading to mortality rates over 70%, if treated conservatively (5,6). Thus it is vital to determine which, if any, older patients with shock should be selected for early revascularization (ERV).

See page 146

Limited randomized trial data exist to direct our management of CS in older adults because they are frequently underrepresented in, or excluded from, clinical trials. Data from the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial suggested that ERV was not superior to initial medical stabilization (IMS) in 30-day mortality among those ≥75 years (7). This subgroup analysis, on the basis of only 56 older adults (24 of whom were randomized to ERV), demonstrated 75% mortality with ERV and 53% mortality with IMS. This led to the American College of Cardiology/American Heart Association Class 1 Guideline recommending ERV limited to those <75 years old, without a recommendation for the elderly.

The SHOCK registry, which included 277 patients ≥75 years, demonstrated that selected older patients had a lower 30-day mortality with ERV versus IMS (which included delayed revascularization) with an adjusted odds ratio of 0.46 (95% confidence interval [CI]: 0.28 to 0.75) (8). Why was there such a significant discrepancy between the registry and trial findings? A review of the SHOCK trial revealed that there were significant imbalances, by chance, in the ejection fraction of those older patients assigned to ERV versus IMS that might have accounted for the apparent lack of treatment effect. On the basis of this and other registry findings, the 2004 American College of Cardiology/American Heart Association STEMI guideline update gave a Class IIa recommendation for ERV for selected patients ≥75 years.

Secondary and subgroup analyses are useful for hypothesis generation but are underpowered and too often, as in the SHOCK trial, misleading and based on chance findings alone. Particularly with respect to underrepresented populations, such as older adults, registries remain important to assess community practice and outcomes. Registries have their problems as well, because patients might be highly selected for invasive care.

In this issue of *JACC: Cardiovascular Interventions*, Lim et al. (9) present a study of elderly patients with MI complicated by CS from the Melbourne Interventional Group (MIG) registry from 2004 to 2007. Their registry includes CS patients who underwent percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction or non–ST-segment elevation myocardial infarction; 45 of 143 patients with CS were age ≥75 years. Although this is a relatively small number, it is on par with prior reports and contributes to the evidence base of PCI use among older CS patients (8). Data from the National Registry of Myocardial Infarction demonstrate an increase in the use of PCI among those CS patients ≥75 years with ST-segment elevation myocardial infarction (from 18.8% to 36.8%) from 1995 to 2004, $p = 0.001$ (10). How representative are the older patients selected for PCI in the MIG registry?

The MIG registry reported an in-hospital mortality rate of 42.2% for older CS patients, which was not statistically different from the rate for younger patients. However, they had limited power to detect significant differences in mortality. The 42.2% mortality rate is substantially lower than that of the American College of Cardiology—National Cardiovascular Data Registry, which contains 143 patients with CS ages 70 to 79 years (in-hospital mortality rate of 64.3%) and 74 patients over age 80 (in-hospital mortality of 81.1%) who underwent PCI (11). In the MIG registry, age was not independently associated with in-hospital mortality, a point the authors highlight. How is it possible that older and younger patients in the MIG registry had apparently similar mortality? This is contrary to nearly every other

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study of MI and CS, which have demonstrated that increasing chronological age is independently associated with a significantly elevated mortality (12–14). In addition to power limitations, we believe there was major bias (likely appropriate) in the clinical selection of elderly patients for invasive management in the MIG registry.

The definition of CS in the MIG registry was similar to previous studies; however, the older patients in their registry seem to have a lower risk profile than prior studies (11). Although both had similar percentages of women and diabetic patients, rates of prior MI (48% vs. 31%) and prior congestive heart failure (28% vs. 13%) were higher among elderly patients in the SHOCK registry. Perhaps most importantly, in the SHOCK registry rates of left main disease were substantially higher (27.8% vs. 7.5%). A recent study has demonstrated that left main patients with CS are better managed with bypass surgery; perhaps these patients in Melbourne were managed by surgery or medical therapy alone (15). It would be useful to know what proportion of patients with CS in each age group was selected for PCI. Data on important prognostic variables (e.g., left ventricular ejection fraction, blood pressure, and cardiac output) were not included in the MIG registry.

It is commendable that rates of stent deployment (86.7%) and use of glycoprotein inhibitors (68.9%) in the MIG registry were much higher than previous studies of interventions in older adults (16). When these interventions were not used in a previous study, there was an increased risk of in-hospital mortality with odds ratios of 2.55 (95% CI: 1.63 to 3.96) and 1.96 (95% CI: 1.30 to 2.98), respectively (11). Although it is tempting to attribute the apparently lower mortality rate to these interventional advances, the use of which is recommended, they have not been proven to improve survival. In the MIG registry the rate of periprocedural complications among older patients was surprisingly low. Most impressive was time from symptom onset to PCI (54.5% <6 h), which is shorter than most studies of PCI in older adults, who often have a delayed presentation and delayed time to the catheterization laboratory (12). It is likely that these older adults were selected on the basis of good prior functional status, "young physiological age," absence of chronic kidney disease, heart failure and dementia, presentation soon after symptom onset with intact cognitive function, and lack of irreversible end-organ damage and deemed to be appropriate candidates for aggressive platelet inhibition and stenting. Lacking randomized trial data demonstrating that ERV improves survival for the elderly, we advocate use of clinical judgment in selecting elderly patients on the basis of the aforementioned characteristics, which were likely used by MIG interventionalists.

We need to define the appropriate selection factors that are used by clinicians but not codified on data forms and to assess the economic, medical, and quality of life impact of ERV and other therapies across a wide range of risk levels. After a 1-year high-risk period for death, in-hospital survivors have good long-term survival rates in the MIG registry and other reports (17). Reassuringly, it seems that most patients who survive the hospital stay for CS have a good quality of life. At 1 year, 87% of shock survivors were in Class I or II heart failure, with no difference in heart failure class on the basis of age, but the number of elderly patients was small (18). It is important that future registries include quality of life measures to assess what often matters most to our patients and their families—survival with intact functional status.

The best therapy for CS remains its prevention, and earlier patient presentation coupled with very early reperfusion is essential. The registry data on CS in elderly patients support the power of clinical judgment compared with unselective use of ERV. At the same time many older adults are subjected to unwanted, costly, painful, and futile life-prolonging efforts. Substantial opportunities remain to improve survival and quality of life or, when appropriate, comfortable death with dignity, for older adults with CS.

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