

Rethinking Cognitive Impairment in the Management of Older Patients With Cardiovascular Disease

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Cognitive impairment and dementia are characterized by diminished memory and ability to complete typical daily activities. There are multiple known causes for cognitive impairment and dementia, including vascular disease and neurodegenerative conditions, such as Alzheimer disease, among others. As the population of the United States ages, the number of people with cognitive impairment will increase significantly to an estimated 13.2 million people in the United States by 2050.¹ Although age is the strongest risk factor for development of cognitive impairment, certain comorbidities may put patients at increased risk for development and progression of cognitive impairment.

In this issue of the *Journal of the American Heart Association (JAHA)*, Gu et al² examined cognitive impairment in a population of patients aged >65 years with non-ST-segment-elevation acute coronary syndrome who underwent coronary angiography with an intention to revascularize as needed.³ Patients with conditions leading to type II myocardial infarctions (MIs) were excluded per trial protocol. Cognitive function was evaluated at baseline and at 1 year after coronary angiography with the Montreal Cognitive Assessment test.⁴ At baseline, almost half of patients in the study were identified as having at least mild cognitive impairment. These patients were less likely to be revascularized after angiography and more likely to have a major adverse event (death, nonfatal MI, urgent unplanned repeated revascularization, stroke, or significant bleeding) at 1 year than patients without cognitive impairment. On reassessment of cognition at the 1-year follow-up, over a third of patients had cognitive decline (Montreal Cognitive Assessment test score decreased by ≥ 2 points). After adjusting for age, sex, and baseline cognitive function, postindex rehospitalizations, MI, and new or worsening heart failure were all associated with an increased risk of cognitive decline during follow-up.

The ADAMS (Aging, Demographics and Memory Study) previously estimated the prevalence of cognitive impairment without dementia to be $\approx 22\%$ in the United States based on a nationally representative cohort of participants aged ≥ 71 years.⁵ Other estimates of cognitive impairment in the general population have ranged from 1% to 29%, largely dependent on the definition of cognitive impairment and sampling methods used.⁶ A recent systematic review identified a 45% increased risk for the development of cognitive impairment among patients with known coronary artery disease.⁷ That patients with cardiovascular disease may be at particularly heightened risk for cognitive impairment is not surprising. Many of the well-established risk factors for coronary artery disease, such as diabetes mellitus, tobacco use, and the metabolic syndrome, have also been identified as potentially modifiable risk factors for development of cognitive decline in older age.^{7,8} Similarly, the Framingham Study found an inverse relationship between blood pressure and cognitive function.⁹ An uncontrolled systolic blood pressure of 160 mm Hg, compared with a target of 120 mm Hg, was associated with a cognitive function equivalent to a patient 10 years older.

What is novel from this report is the high prevalence of cognitive impairment in $\approx 50\%$ of patients who underwent coronary angiography and were deemed candidates for revascularization; this is after excluding patients who may have had type II “demand” MIs as a result of other medical conditions, such as active infection, that may affect cognition. These findings raise significant implications for healthcare decisions and delivery. Patients with cognitive impairment are infrequently consented into randomized cardiovascular clinical trials; thus, the evidence of benefit for cardiovascular medications and procedural interventions is much weaker. This can be especially problematic in older patients with

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cognitive impairment for whom the benefit of invasive cardiac treatment must be weighed with the higher potential risks associated with these treatments. Treatment risks, such as periprocedural bleeding or drug-drug interactions, can be particularly magnified in patients with cognitive impairment.

Beyond the risks and benefits of therapies, older patients with cognitive impairment may also have different goals of medical care. Although treatment of underlying pathological features and prevention of recurrent ischemic events remain important for the patient with acute coronary syndrome, prioritizing time at home and avoiding precipitants of further cognitive decline may supersede life prolongation goals for patients with cognitive impairment. Observational data for hospitalized patients with cognitive impairment show an increased risk of delirium while hospitalized, increased length of stay, and increased mortality.^{10,11} Perhaps partially because of these considerations, this study echoes prior studies in showing lower revascularization rates among older patients with cognitive impairment; clinicians appeared to elect a more conservative approach after the anatomical features were clarified during coronary angiography.^{12–14} Which patients with acute coronary syndrome might benefit from percutaneous or surgical revascularization needs to be carefully evaluated because patients with cognitive impairment are at significantly higher risk of downstream adverse events. Assessment of patient frailty, of which cognitive impairment is a key component, should be routine in preprocedural evaluations of patients with coronary artery disease. Observational studies, to date, have shown that frail patients have a higher risk for functional decline, major adverse coronary events, and mortality after cardiac surgery.^{15,16} The FRAGILE (Off-Pump Versus On-Pump Coronary Artery Bypass Grafting in Frail Patients) trial will assess outcomes of on- versus off-pump coronary artery bypass grafting among frail and prefrail patients.¹⁷ As treatment options continue to evolve, it becomes increasingly important to objectively evaluate patient-centered outcomes in this growing patient population.

Cognitive decline after hospitalization is not a finding unique to patients with acute coronary syndrome. Prior work has demonstrated long-term cognitive impairment in patients who experience delirium, those who receive sedation for mechanical ventilation or invasive procedures, and patients requiring critical care while hospitalized.^{18,19} More important, Gu et al² also found a significant association between rehospitalizations, including recurrent MIs, and cognitive decline. This highlights the need for the guideline-directed treatment of not only the acute event but also of modifiable risk factors that prevent recurrent cardiovascular events and, more generally, prevent rehospitalization. Medication adherence is critical to preventing recurrent cardiovascular events, and older individuals with cognitive impairment may be

particularly vulnerable to nonadherence or medication confusion. Among older patients with MI, we have observed interhospital variation in postdischarge secondary prevention medication adherence,²⁰ suggesting that targeted in-hospital interventions can have significant impact on both short- and long-term medication adherence. Ensuring close outpatient follow-up postdischarge may also allow clinicians to closely monitor adherence, head off post-MI complications, and fill any gaps in the transition of care.^{21,22} Novel mechanisms of follow-up and social support may be particularly impactful for patients with cognitive impairment to maximize home time and quality of life.

Cognitive impairment in patients with cardiovascular disease represents a complex relationship between the aging process, common modifiable risk factors, and acute events that may lead to a more rapid decline in cognition. This patient population represents one with unique challenges to treatment of cardiovascular disease, but also a population in which recurrent hospitalizations and cardiovascular events may be particularly deleterious. Similar to cardiovascular disease, the treatment of cognitive impairment requires treatment and consideration long before symptoms are present. Although the exact mechanistic link between the 2 disease processes remains unclear, it is evident that common modifiable risk factors are an important target for primary prevention of both. Early recognition and treatment of diabetes mellitus, hypertension, hyperlipidemia, obesity, and tobacco use may help in the development and progression of both cardiovascular disease and cognitive impairment. Ongoing work is needed to fully elucidate the relationship between these 2 disease processes and to clarify the best ways to care for this complex patient population.

Disclosures

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