Stable Coronary Artery Disease in the Age of Geriatric Cardiology*



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he extrapolation of evidence generated in younger adult populations to the geriatric population is fraught with limitations and hazards, given unique vulnerabilities that impact the safety and efficacy of diagnostic approaches and treatments, distinct health care needs, and heterogeneity in patient priorities. This underlies the need for geriatric cardiology, a subdiscipline of cardiology that has "come of age" in recent years. Geriatric cardiology is focused on adapting cardiovascular care to the unique needs of older adults, and provides a framework for navigating the complexity of cardiovascular diseases within the context of advanced age and associated geriatric syndromes such as frailty, cognitive impairment, and polypharmacy, among others.1

As the population ages, clinicians are increasingly faced with making decisions about how to manage coronary artery disease (CAD) in older adults. Importantly, there are well-established differences in atherosclerotic burden, procedural and technical complexity, and procedural risk among older adults.² Consequently, there is variability in procedural success and increased risk of complications among older adults, and revascularization may be deferred entirely in some cases. There is also a paucity of evidence to guide decision making regarding management of CAD in older adults. Data are particularly scarce for older adults with stable CAD–a condition that has been extensively studied through myriad clinical trials that have systematically excluded older adults.³ Indeed, of the dozens of randomized trials investigating invasive treatment vs medical therapy for the treatment stable CAD, only one has had a mean age >67 years and was conducted more than 2 decades ago.⁴

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In this issue of the Journal of the American College of Cardiology, within this context, the analysis of health status of more than 600 older adults with stable CAD from the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial by Nguyen et al⁵ represents a landmark contribution to the existing literature. The ISCHEMIA trial randomized 5,179 adults (median age 64 years) with moderate or severe ischemia to an initial invasive strategy vs a conservative strategy, finding no significant difference between the 2 strategies for the primary outcome of cardiovascular death, myocardial infarction (MI), or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest regardless of age.⁶ The only potential benefit in a clinical endpoint with an invasive strategy (observed across all ages including older adults) was in reducing future nonprocedural MI (at 75 years of age, HR: 0.62; 95% CI: 0.45-0.85), at the cost of increasing procedural MI events (at 75 years of age, HR: 3.68; 95% CI: 1.85-7.32).⁵ Of note, the ISCHEMIA trial enrolled the most older adults in a randomized clinical trial of stable CAD to date. The authors should be applauded for improving our understanding of the impact of an invasive vs

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conservative management strategy on symptoms, function, and quality of life specifically in older adults. Quantifying the effect of therapeutic decisions on how patients feel is a key patient-centered outcome for all patients, with especially heightened importance for older adults.7 While the authors showed that older adults (\geq 75 years of age) experienced a reduction in angina frequency with an invasive strategy, they observed an attenuated benefit for both angina-related health status and quality of life (via Seattle Angina Questionnaire-7 and EQ-5D scores) compared with younger adults. Taken together, data from the ISCHEMIA trial indicate that an invasive strategy in older adults with stable CAD can reduce future spontaneous MI and angina frequency but does not have a substantial impact on quality of life. Results here are critical to further informing the risk-benefit calculus of management decisions in older adults presenting with stable coronary disease, in which benefits must be balanced against upfront procedural risks and risk for complications such as bleeding or acute renal injury. Given the observation that older adults in the ISCHEMIA trial achieved improvements in angina-related health status and overall quality of life regardless of strategy, these findings indicate that managing stable CAD in older adults is possible and that the approach is a preference-sensitive decision that thus requires careful deliberation and patient involvement.

It is important to recognize that the ISCHEMIA trial enrolled a relatively healthier subset of older adults than that seen in routine practice, excluding patients with low ejection fraction (\leq 35%) and enrolling participants with a relatively low prevalence of multimorbidity (23.4%). This healthy selection bias is a long-standing issue for nearly all randomized controlled trials in cardiovascular medicine that must be considered when interpreting the findings.⁸ Generalizability concerns are particularly relevant in older adults, in which the presence of geriatric conditions such as multimorbidity, polypharmacy, cognitive impairment, and/or frailty among others can modify individual patient responses (both benefit and harm) to cardiovascular therapies.^{9,10} Even among a relatively healthier older adult population, a smaller proportion of older adults (<70% in total) in the invasive arm underwent revascularization compared with their younger counterparts, a finding more commonly attributed to unsuitable anatomy for older adults compared with younger adults. Based on this observation, it is possible that a sicker multimorbid population would have been even less likely to undergo revascularization, further attenuating any potential benefit of an "invasive" strategy. On the

other hand, there may be reasons to consider the possibility of greater effect in a sicker subpopulation in select scenarios. For example, opting for revascularization instead of adding/increasing antianginal medications in a frail older adult with polypharmacy at risk for falls may be reasonable in some cases. Indeed, in some situations, a one-time intervention with upfront risk may be preferred over alternative strategies like long-term pharmacotherapy, which also has attendant risks.¹¹

When uncertainty exists around the potential benefits and harms of a given treatment within the complex milieu of biological aging, decision making for clinicians and older patients can be challenging. The authors appropriately emphasize the importance of shared decision making among older adults considering revascularization and the need for shared decision-making tools that incorporate the influence of geriatric conditions on person-centered outcomes. A recently proposed "Consider, Listen, Decide" framework recommends that clinicians consider the clinical context of the individual patient, listen to the patient's goals of care and priorities, and decide on the treatment approach that best aligns with the patient's health goals.⁴ Clinical context, elicitation of patient goals and priorities, and decision making can be challenging when caring for older adults with cardiovascular disease, but fortunately this has been a major area of development over the past several years (Figure 1). For clinical context, the domain management approach for providing care to older adults offers a scaffold that enumerates multiple domains and subdomains of health that are relevant to older adults such as cognition, physical function, and the social environment.¹² Further investigation is required to clarify the influence of various geriatric conditions on the risks and benefits of both procedural interventions and pharmacologic alternatives. For eliciting patient goals and priorities, Patient Priorities Care is a feasible and effective approach to assist clinicians and patients with aligning health care decisions with the outcomes that patients want to achieve13-this is especially important given substantial heterogeneity among older adults regarding their health priorities, preferences, and goals of care, which have implications for identifying the optimal treatment for older adults. For decision making, decision aids that enumerate and quantify risks and potential benefit can be helpful; and N-of-1 trials have been proposed as an innovative approach that can generate individual-level evidence to facilitate informed person-centered decisions with greater precision.¹⁴ While significant hurdles remain, the work by Nguyen et al⁵ is a major advancement in the



quest toward improving the evidence to inform decision making in older adults with stable CAD. As clinicians and patients embrace the complexity at the intersection of aging and cardiovascular disease, we have the opportunity to advance the care of our most vulnerable older patients.

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