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What do the recent American Heart Association/American College of Cardiology Foundation Clinical Practice Guidelines tell us about the evolving management of coronary heart disease in older adults?

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Abstract

Biological aging predisposes older adults to increased cardiovascular disease (CHD) and greater disease complexity. Given the high age-related prevalence of CHD and age-related compounding factors, the recently updated American Heart Association/American College of Cardiology Foundation CHD-related guidelines increased their focus on older patients. These guidelines are predominately evidence-based (using data from quality randomized clinical trials) and are organized to delineate medications and procedures that best treat particular cardiovascular diseases. While such rationale and thought work well in young and middle aged adults, they become problematic in patients who are very old. Data pertaining to adults aged ≥ 80 are virtually absent from most randomized clinical trials, and even in the instances when very old patients were included, eligibility criteria typically excluded candidates with co-morbidities and complexities of customary CHD patients. While medications and interventions yielding benefit in clinical trials should theoretically produce the greatest benefits for patients with high intrinsic risk, age-related cardiovascular complexities also increase iatrogenic risks. Navigating between the potential for high benefit and high risk in “evidence-based” cardiovascular management remains a key Geriatric Cardiology challenge. In this review we consider the expanded Geriatric Cardiology content of current guidelines, acknowledging both the progress that has been made, as well as the work that still needs to be accomplished to truly address the patient-centered priorities of older CHD patients.

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Keywords: Cardiovascular disease; Guidelines; Elderly patient

1 Introduction

Biological aging predisposes older adults to cardiovascular disease.^[1] In the United States, the population aged 65 years and older accounts for more than 80% of cardiovascular disease deaths and 85% of cardiovascular disease hospitalizations, including 62% of hospitalizations for myocardial infarction and 77% of hospitalizations for heart failure.^[2,3] Advancing age is also associated with greater cardiovascular disease complexity. Coronary heart disease (CHD) is more frequently associated with other cardiovascular diseases (e.g., with heart failure, arrhythmia, and/or valvular heart disease), and also more frequently associated with non-cardiac diseases, patterns that tend to complicate

management and worsen outcomes.^[4] Older CHD patients are also more likely to be taking multiple medications, to be hampered by physical limitations (cognitive and functional) and to be coping with many additional health dynamics (e.g., chronic pain, poor sleep) that compound cardiovascular risks and pose management challenges.

Given the high age-related prevalence of CHD and age-related compounding factors, the recently updated American Heart Association/American College of Cardiology Foundation (ACCF/AHA) CHD-related guidelines included increased focus on older patients. These guidelines are predominately evidence-based (using data from quality randomized clinical trials) and are organized to delineate medications and procedures that best treat particular cardiovascular diseases.^[5] While such rationale and thought work well in young and middle aged adults, they become problematic in patients who are very old. Data pertaining to adults aged ≥ 80 are virtually absent from most randomized clinical trials, and even in the instances when very old patients were included, eligibility criteria typically excluded candidates with comorbidities and complexities of custo-

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mary CHD patients. Therefore, a medication judged to be effective according to guidelines criteria may produce unanticipated harm in very old age, particularly for patients with multimorbidity, polypharmacy, and other typical age-related health complexities. “Geriatric cardiology” addresses age-related elements as fundamental components in cardiovascular care. The inclusion of geriatric cardiology perspectives to the guidelines corroborates the growing awareness that aging broadly impacts management decisions and outcomes.

Cardiovascular disease is both more common and more perilous as a function of advanced age. While medications and interventions yielding benefit in clinical trials should theoretically produce the greatest benefits for patients with high intrinsic risk, age-related cardiovascular complexities also increase iatrogenic risks. Navigating between the potential for high benefit and high risk in “evidence-based” cardiovascular management remains a key Geriatric Cardiology challenge.

2 Stable ischemic heart disease

The 2012 guideline for the diagnosis and management of patients with stable ischemic heart disease^[6] defines older adults as those > 75 years of age, and includes a small section focused specifically on their care. The text acknowledges that older patients are more likely to have diffuse and severe disease coronary atherosclerosis with a higher prevalence of three-vessel and left main coronary artery disease. The guideline recognizes that common co-existing conditions makes diagnosis more difficult, including the limited capacity of older adults to exercise and their high prevalence of baseline electrocardiographic changes that render exercise test data less reliable. The utility of the Duke Treadmill Score as a prognostic index is similarly limited, both because of physical limitations of most old adults and also due to their higher prevalence of stable ischemic heart disease that diminishes the utility of a function-based test to stratify risk. Relative benefits of imaging modalities to enhance diagnosis and prognosis of CHD are highlighted.

The guidelines cite a number of studies showing the less frequent use of evidence-based therapies in older adults including early invasive procedures, anti-coagulants, beta blockers, and glycoprotein IIb/IIIa antagonists, likely related to challenges of pharmacotherapy stemming from polypharmacy (and drug interactions) as well as age-related differences in drug bioavailability and elimination. Given these concerns, a conservative approach to coronary angiography is generally advised, especially given higher age-related risks of contrast-induced nephropathy and increased mor-

bidity and mortality risks associated with coronary artery bypass graft surgery.

Randomized controlled trial data comparing guideline-based medical therapy with myocardial revascularization in older patients are also reviewed. Whereas revascularized patients showed greater improvements in symptoms in the early months, improvements were comparable in symptoms and other quality-of-life measures in both groups over the long term, providing additional rationale for non-invasive management. There is considerable evidence that elderly patients have higher mortality rates following percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery than do younger patients, but the available data are highly variable. Thus, the guideline recommendation for patients with stable ischemic heart disease includes initial management that essentially overlaps with guideline-based medical therapy for older adult patients of any age. However, given the concerns about higher mortality rates associated with revascularization, particularly in patients older than 75 to 80 years, revascularization is recommended only after careful consideration of patient preferences and desired outcomes, functional capacity, quality-of-life and end-of-life issues, as well as therapeutic alternatives.

3 Unstable angina/Non-ST-elevation myocardial infarction

The 2012 ACCF/AHA Focused Update^[7] incorporated into the ACCF/AHA 2007 Guidelines^[8] for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction includes a section that addresses older adults as a distinct management process. Five class I recommendations are provided: (1) older patients with Unstable Angina/Non-ST-Segment Elevation Myocardial Infarction (UA/NSTEMI) should be evaluated for appropriate acute and long-term therapeutic interventions in a similar manner as younger patients with UA/NSTEMI, (Level of Evidence: A); (2) decisions on management of older patients with UA/NSTEMI should not be based solely on chronologic age but should be patient-centered, with consideration given to general health, functional and cognitive status, comorbidities, life expectancy, and patient preferences and goals, (Level of Evidence: B); (3) attention should be given to appropriate dosing (i.e., adjusted by weight and estimated creatinine clearance) of pharmacological agents in older patients with UA/NSTEMI, because they often have altered pharmacokinetics (due to reduced muscle mass, renal and/or hepatic dysfunction, and reduced volume of distribution) and pharmacodynamics (increased

risks of hypotension and bleeding), (Level of Evidence: B); (4) older UA/NSTEMI patients face increased early procedural risks with revascularization relative to younger patients, yet the overall benefits from invasive strategies are equal to or perhaps greater in older adults and are recommended, (Level of Evidence: B); and (5) consideration should be given to patient and family preferences, quality-of-life issues, end-of-life preferences, and socio-cultural differences in older patients with UA/NSTEMI, Level of Evidence: C.

Overall, the recently updated UA/NSTEMI guidelines acknowledge the complexity of older CHD patients, but assert that evidence-based standards for younger adults are often still effective. However, they also emphasize that management of older CHD patients must incorporate age-related issues into cardiovascular management choices: i.e., medical and cognitive status, bleeding risk and other risk of interventions, anticipated life expectancy, and patient or family preferences.

4 STEMI

The 2013 ACCF/AHA Guideline for the Management of STEMI^[9] is a revision of the 2009 Focused STEMI Updates.^[10] The older population is noted to present special challenges for diagnosis and management, including delays in or lack of reperfusion, increased risk of antithrombotic therapy, and presence of comorbidity and renal impairment which require dosing adjustment.

Although the clinical trials frequently have a limited enrollment of older populations, treatments that are effective in younger patients are usually indicated in the older adults, with the caveat that older adults more often have absolute or relative contraindications to their use. The guidelines recommend appropriate boundaries of care within the context of individual co-morbidities, frailty, and advanced-care directives. Some medications are specifically mentioned as not recommended due to excessive iatrogenic risks, i.e., prasugrel for PCI treated patients, 300 mg loading dose of clopidogrel in fibrinolytic-treated patients.

In the CRUSADE Quality Improvement Initiative (2004–2006) 7% of eligible STEMI patients did not receive reperfusion therapy, with the factor most strongly associated with lack of providing reperfusion in these patients being increasing age.^[11] Nonetheless, even very elderly patients have reasonable post-infarction outcomes when treated aggressively with reperfusion therapy, although individual circumstances vary.

Both the GWTG Quality Improvement Program and a reperfusion acute myocardial infarction initiative in North

Carolina demonstrated that programs designed to systematize care across integrated regional centers can lessen disparities and improve the care of elderly patients with STEMI.^[12] Currently, longer delays to Emergency Medical activation are common among older adults, often due to atypical, symptoms and/or lack of symptom recognition.

5 PCI

The 2011 guideline for PCI^[13] acknowledges that older adults constitute a growing proportion of patients considered for PCI. In one series examining trends over 25 years, the proportion of patients undergoing PCI who were 75–84 years of age doubled and those older than age 85 years increased fivefold. Older age is a strong predictor of mortality following PCI and older adults present with a substantially higher clinical risk profile. Nonetheless, the guidelines stress that angiographic success rates and clinical benefits of PCI in older adults are similar to those in younger patients; thus, the higher absolute benefit associated with older age compensates for the higher absolute risk of adverse outcomes. Nonetheless the increased risks of complications such as major bleeding and stroke mandate careful consideration of the benefits and risks of PCI for individual elderly patients.

6 Coronary artery bypass graft surgery

The 2011 guideline for coronary artery bypass graft surgery^[14] defines the term “elderly” as ≥ 80 years of age. As in prior coronary disease subsets, older adults, compared with younger subjects, are more likely to have severe coronary artery disease (left main or multi-vessel disease), left ventricular systolic dysfunction, concomitant valvular disease, and to previously have had a sternotomy. Frequent co-morbid conditions include diabetes mellitus, hypertension, chronic obstructive pulmonary disease, peripheral arterial disease and azotemia. Consequently, elderly patients have a higher perioperative risk of morbidity and mortality than younger patients.

Operative mortality among elderly patients ranges from 2.6% at ages older than 75 to 11% at ages older than 80 years^[15,16] undergoing urgent surgery. In several retrospective studies, a substantially higher in-hospital mortality rate is reported among octogenarians than among younger patients. In the National Cardiovascular Network, which included 4,743 octogenarian patients, the in-hospital mortality rate for octogenarians was 8.1% compared with 3% for the remaining population.^[17] Retrospective studies also showed that octogenarians have a higher incidence of neurological

complications, renal failure, respiratory failure and gastrointestinal complications than younger patients.^[15,17,18] Consistently, octogenarians have longer lengths of stay, long durations of intensive care, and are less likely to be discharged home. In the New York state registry, the length of stay was 8.5 days for patients younger than age 50 years compared with 14.1 days for those ≥ 80 , with discharge-to-home rates of 96% and 52% respectively.^[16]

Despite their higher rates of in-hospital morbidity and mortality, the majority of octogenarians achieve functional improvement following coronary artery bypass graft surgery. Two studies of patients > 80 years of age demonstrated improvements in quality of life.^[19,20] In one study, angina relief and quality-of-life improvement scores did not differ between patients older and younger than 75 years of age. Of 136 octogenarians following coronary artery bypass grafting surgery, 81% felt that they were left with little or no disability in their daily activities and 93% reported substantial symptomatic improvement at an average of 2 years post-operatively.^[19]

7 Discussion

While U.S. CHD guidelines have evolved in their specific inclusion of age-based dimensions of care, many unresolved relevant elements of care remain. Even the precise definition of age remains ambiguous, with variance between the different guidelines in the number of years considered as “old age” and/or components of health correlated to years of life that impact on management decisions. Likewise, age is usually mentioned as a set point, rather than as a continuum that can fluctuate in relation to accumulating years as well as in relation to variations in aggregate health and social dynamics.^[4]

Clinical trial endpoints constituting the basis of most guidelines recommendations are also rarely aligned to an aging perspective. Whereas most trials underlying CHD guidelines assess mortality endpoints, older adults may not view length of life as their greatest concern. Health goals for many CHD patients with chronic illness include independence in daily living; improved functional capacity, particularly the ability to ambulate; decreased hospitalizations and symptoms, i.e., prolongation of symptom-free life. Therefore it remains ironic that the concepts of patient-centered care or patient preferences which are appropriately emphasized as a key component of management choices can rarely be informed with relevant data.

The guidelines often extrapolate from the standards emphasized for younger adults with some recommendations for precaution (e.g., renal and weight-dose adjustments).

However, standard recommendations for younger populations often produce untoward effects that remain relatively poorly demarked. For example, beta blockers may limit chronotropy and exercise performance and potentially increase the need for pacemaker implantation. Nitrate drugs, despite symptom relief, may be associated with an increase in fall risk and syncope.

Other interventions effective in younger patients may adversely affect older adults; for example, despite the benefits of drug-eluting stents and intensive anti-platelet therapy for younger adults,^[21] they substantially increase the bleeding risk at elderly age. This is particularly complicated for older adults prone to atrial fibrillation and thromboembolic disease for which anti-thrombin therapy may be indicated, further exacerbating bleeding risk.

Perhaps under-emphasized in all guidelines is the necessity for patient education designed to foster adherence to medications, diet, physical activity and other health-promoting behaviors. It remains ironic that trials often do not collect data most pertinent to older patients' concerns, but it is likely that if patients understood which medications best achieved independence, function, and high quality of life, it would reinforce compliance. Patient and family/caregiver education is highly relevant for older adults.

Cardiac rehabilitation services also merit added emphasis as a component of CHD care that is particularly likely to benefit the many older CHD patients. Paradoxically, cardiac rehabilitation is substantially under-utilized among older adults with CHD despite strong evidence that facility and/or home-based cardiac rehabilitation programs lessen morbidity and mortality, improve quality of life and functional capacity, and decrease readmissions and healthcare costs in frail to robust older adults.^[22] Physician recommendation is the strongest determinant of cardiac rehabilitation utilization.

As the guidelines are serially updated, it is likely the focus and sophistication in relation to age will grow. Tiered management, stratified to better account for a continuum of comorbidity, frailty, medications, and other components of health will likely evolve, adapting standards of evidence-based care to older adults. Specific medication and procedural strategies to improve CHD management in relation to age will also likely evolve, targeting goals to mitigate bleeding and other iatrogenic risks without forgoing therapeutic benefits. Diagnostic sensitivity and specificity will also likely improve, potentially linking functional and/or serological indices to imaging to better predict which older CHD patients may benefit from therapy despite higher age-related therapeutic risks. The consistent inclusion of age as a relevant dimension of care appears an important first

step toward improved management of the burgeoning population of senior adults who are intrinsically prone to cardiovascular disease.

8 Summary

A patient-centered approach, i.e., management personalized to each patient's situation, is pivotal in the diagnostic and therapeutic considerations of coronary heart disease in older adults.

A systematic approach is requisite to incorporate age-related complexities into clinical decision-making. Cardiovascular risks must be assessed in the context of aggregated age-related risks, determining realistic goals that incorporate each patient's overall health circumstances to determine the risks and the benefits of specific options of care. These include cardiac and non-cardiac co-morbidities, functional capacity (physical and cognitive), pain, and quality of life factors, all highly relevant in selecting patients most likely to benefit from different therapeutic choices.

Patient-centered treatment goals must also address quality of life, function, independence, and avoidance of adverse events. More data are needed from a broad range of older adults to better determine specific thresholds for medical and invasive interventions, development of strategies to minimize adverse events, and the incorporation of complex co-morbidities into risk/benefit ratios.

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