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AHA/ACC/AGS SCIENTIFIC STATEMENT

Knowledge Gaps in Cardiovascular Care of the Older Adult Population

A Scientific Statement From the American Heart Association, American College of Cardiology, and American Geriatrics Society

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ABSTRACT

The incidence and prevalence of most cardiovascular disorders increase with age, and cardiovascular disease is the leading cause of death and major disability in adults ≥75 years of age; however, despite the large impact of cardiovascular disease on quality of life, morbidity, and mortality in older adults, patients aged ≥75 years have been markedly underrepresented in most major cardiovascular trials, and virtually all trials have excluded older patients with complex comorbidities, significant physical or cognitive disabilities, frailty, or residence in a nursing home or assisted living facility. As a result, current guidelines are unable to provide evidence-based recommendations for diagnosis and treatment of older patients typical of those encountered in routine clinical practice. The objectives of this scientific statement are to summarize current guideline recommendations as they apply to older adults, identify critical gaps in knowledge that preclude informed evidence-based decision making, and recommend future research to close existing knowledge gaps. To achieve these objectives, we conducted a detailed review of current American College of Cardiology/American Heart Association and American Stroke Association guidelines to identify content and recommendations that explicitly targeted older patients. We found that there is a pervasive lack of evidence to guide clinical decision making in older patients with cardiovascular disease, as well as a paucity of data on the impact of diagnostic and therapeutic interventions on key outcomes that are particularly important to older patients, such as quality of life, physical function, and maintenance of independence. Accordingly, there is a critical need for a multitude of large population-based studies and clinical trials that include a broad spectrum of older patients representative of those seen in clinical practice and that incorporate relevant outcomes important to older patients in the study design. The results of these studies will provide the foundation for future evidence-based guidelines applicable to older patients, thereby enhancing patient-centered evidence-based care of older people with cardiovascular disease in the United States and around the world. (J Am Coll Cardiol 2016;67:2419–40)

The American Heart Association, the American College of Cardiology, and the American Geriatrics Society make every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

The prevalence of cardiovascular disease (CVD) increases progressively with age, and people ≥65 years of age account for more than half of all cardiovascular hospitalizations and procedures in the United States, as well as ≈80% of all cardiovascular deaths (1). Although people ≥75 years old account for only ≈6% of the total population, >50% of cardiovascular deaths occur in this age group (1). Indeed, cancer is the leading cause of death among U.S. adults 18 to 74 years of age, and it is only after age 75 years that CVD becomes the dominant cause of mortality (1,2). The global burden of CVD is increasing, primarily because of the aging of the population, and men and women ≥80 years of age account for a disproportionate number of cardiovascular deaths (3). CVD is also a major cause of chronic disability, loss of independence, and impaired quality of life among older people (4,5). Despite the high prevalence, morbidity, and mortality of CVD in older adults, most randomized clinical trials have either explicitly excluded older adults or have enrolled only relatively healthy older patients with few comorbidities or functional impairments (6,7). As a result, the generalizability of the results of most major clinical trials to older patients, especially those >75 years of age with multimorbidity, is uncertain (6,8). Moreover, because of age-related changes in cardiovascular structure and function (9,10), coupled with changes in other organ systems, including the kidneys, liver, skeletal muscle, and brain, older patients are at increased risk for complications related to pharmacological and nonpharmacological interventions. It therefore should not be assumed that outcomes reported in clinical trials involving younger and healthier patients are applicable to older adults who have fundamental alterations in risks and potential benefits of diagnostic, therapeutic, and preventive interventions. Furthermore, few clinical trials have assessed outcomes important to older adults, such as quality of life, maintenance of independence, and physical and cognitive function (8). Current evidence-based practice guidelines suffer inherent gaps in providing recommendations for managing older adults with CVD, the majority of whom would not have been eligible for participation in most of the major clinical trials. The objectives of this American Heart Association (AHA) scientific statement are to summarize current guideline recommendations as they apply to older adults, identify critical gaps in knowledge that preclude informed decision making, and recommend future research to close existing knowledge gaps, thereby leading to enhanced care and outcomes for the expanding population of older adults with cardiovascular disorders.

METHODS

Current American College of Cardiology (ACC)/AHA and American Stroke Association (ASA) practice guidelines (Appendix) relevant to older adults were reviewed by at least 2 members of the writing committee. Content and recommendations that explicitly focused on older patients were identified and summarized. Pertinent gaps in knowledge that limited the applicability of guideline recommendations to older adults, especially those >75 years of age and those with multimorbidity or other complexities of care (e.g., cognitive impairment, nursing home residence), were identified, and specific research recommendations for overcoming these knowledge gaps were proposed. The initial draft of the manuscript was reviewed by all members of the writing committee to identify additional knowledge gaps and research needs. The manuscript was subsequently reviewed by 16 content experts representing the ACC, AHA, and American Geriatrics Society. All comments and suggestions were addressed, and the revised manuscript was reviewed and approved by all members of the writing group before submission for publication.

KNOWLEDGE GAPS ACROSS GUIDELINES

Several common themes pertaining to knowledge gaps extend across most of the ACC/AHA and ASA guidelines.

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In general, the studies on which the guidelines are based enrolled few older adults or included older patients with few comorbidities who were not representative of the older population treated for CVD in the community. The importance of assessing relevant domains beyond chronological age, such as frailty and cognitive function, and the incorporation of patient preferences into shared decision making have not been assessed adequately. The utility of all cardiac preventative measures, diagnostic tests, and therapeutic interventions, including medications, invasive procedures, and other programs (e.g., cardiac rehabilitation) in the management of older patients with CVD warrants careful scrutiny, especially in the context of multimorbidity, polypharmacy, functional limitations, and frailty (11).

Recommendations to Close Knowledge Gaps Across Guidelines

- Intensive efforts are needed to recruit representative older adults in clinical cardiovascular research. There should be mandatory reporting of enrollment, assistance with transportation and other challenges that limit the inclusion of older adults, and detailed postmarketing surveillance. Studies that include the full spectrum of community-dwelling and institutionalized older adults are essential, especially in light of the marked heterogeneity of the older population. In particular, older patients with multiple comorbid conditions, functional and cognitive deficits, and frailty should be actively included in clinical studies. Studies should also address sex, racial/ethnic, and cultural issues through prespecified enrollment criteria and subgroup analyses. Methodologies for increasing participation of older adults in clinical research should be explored (e.g., U.S. Food and Drug Administration labeling of drugs and devices as being approved or not approved for use in elderly patients).
- In addition to assessing conventional clinical outcomes, future studies should incorporate health status, quality of life, functional capacity (e.g., ability to perform activities of daily living and instrumental activities of daily living), maintenance of independence, and cognitive function.
- Similarly, there is a need for studies that assess cost-effectiveness, value, and resource utilization in the diagnosis and treatment of older adults with or at risk for CVD and with reference to specific patient-centered clinical outcomes.
- Models for integration of patient preferences, values, and goals of care into the decision-making process for management of CVD in older adults are needed. Such models should also involve caregivers and significant others and must anticipate and incorporate methods for overcoming impediments to decision making, such as cognitive impairment and sensory deficits. Research is also needed to develop simple, patient-friendly tools that enable care providers to integrate patient preferences and goals of care into the decision-making process. Similarly, research is needed to better define subgroups of patients who, as a result of advanced disability, cognitive impairment, or other factors, may be unlikely to derive significant benefit from aggressive therapies and who may be better served by referral for palliative care or hospice.
- Studies are needed to develop more accurate models for assessing prognosis and life expectancy in older adults with CVD in the context of multiple chronic conditions and heterogeneous functional and cognitive status. Better tools are needed to more accurately characterize domains of health in older adults, and studies are needed to evaluate strategies for incorporating data on health status and prognosis into the decision-making process. Similarly, tools and biomarkers are needed to predict the trajectory of cognitive impairment, disability, and frailty, because these factors often influence clinical decision making.
- Additional studies are needed to delineate optimal strategies for prevention of CVD in older adults, including patient-centered blood pressure, lipid, and diabetes mellitus goals, methodologies and targets for enhancing fitness, and novel approaches to primary and secondary CVD prevention.
- Studies are needed to evaluate rehabilitation services (both traditional cardiac rehabilitation and therapies focused on strength, balance, and gait training) for optimization of clinical and functional outcomes.

CORONARY ARTERY DISEASE

ST-Elevation Myocardial Infarction and Non-ST-Elevation Acute Coronary Syndromes

Current Recommendations

The "2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction," a revision of the 2004 ST-elevation myocardial infarction guideline and the 2007 and 2009 focused ST-elevation myocardial infarction updates, is, by design, narrow in scope to provide a focused tool for providers (12–15). Although it is acknowledged that older patients often present challenges for diagnosis and treatment, few recommendations advocate alterations in management in patients of advanced age.

The "2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes" includes a separate section that addresses management of older adults (16). Three Class I and 2 Class IIa recommendations are provided. Among these, it is noted that "management decisions for older patients with

NSTE-ACS [non-ST-elevation acute coronary syndrome] should be patient centered, and consider patient preferences/goals, comorbidities, functional and cognitive status, and life expectancy (*Level of Evidence: B*)." The need for dosage adjustment of many medications to reduce the risk of adverse effects, such as bleeding, is acknowledged, as is the increased risk associated with revascularization procedures in older adults relative to younger patients. It is also noted that the potential benefits of aggressive treatment in older adults with NSTE-ACS are often equal to or greater than those in younger people, and it is emphasized that such therapies should not be withheld solely on the basis of age.

The NSTE-ACS guideline acknowledges that older patients present complex challenges because of atypical symptomatology, high prevalence of cardiac and noncardiac comorbidities, age-related alterations in cardiovascular anatomy and physiology, and increased risk for adverse drug events and interactions caused by polypharmacy. It is also acknowledged that older patients have been underrepresented in clinical trials and that numerous studies have documented that advanced age is associated with lower use of pharmacological and invasive therapies (17,18). Nonetheless, caution is required in treating older patients with medications because of alterations in drug metabolism and distribution that result from age-related changes in renal and hepatic function and alterations in body composition, especially reduced lean body mass (16).

Recommendations to Close Knowledge Gaps

[Note: Recommendations marked with an asterisk (*) also apply to the section on stable ischemic heart disease, percutaneous coronary intervention, and coronary artery bypass graft surgery.]

- Studies are needed to assess the benefits, risks, intensity, and duration for pharmacological agents, including antiplatelet agents, statins, β-blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and mineralocorticoid antagonists among older patients with acute coronary syndrome (ACS), with attention to multimorbidity and polypharmacy.*
- Additional studies are needed to define the risks and benefits of conservative versus invasive care in older patients with ACS, including the impact on quality of life, particularly in the setting of multimorbidity, frailty, or limited life expectancy.*
- There is a need for risk-stratification tools relevant to older adults to identify patients most likely to derive benefit from aggressive interventions.*
- Studies that assess age-associated alterations in platelet function and hemostasis are needed. Comparative effectiveness studies are needed to assess the benefits and risks of different antiplatelet agents, alone and in combination with warfarin or other antithrombotic agents, in older patients with ACS.*
- Comparative effectiveness studies are needed to assess the benefits and risks associated with drug-eluting stents versus bare-metal stents for primary percutaneous coronary intervention (PCI) in older patients with ACS, including the impact on long-term outcomes (given the need for longer dual-antiplatelet therapy with drug-eluting stents).*
- Studies are needed to assess the use of newer high-sensitivity troponin assays in older patients, including identification of appropriate diagnostic cut points and the comparative effectiveness of high-sensitivity assays versus conventional assays in the diagnosis, management, and outcomes of older patients with suspected ACS.
- Studies are needed to better clarify the appropriate management and subsequent prognosis of patients with type 2 myocardial infarction (i.e., elevation of cardiac biomarkers caused by imbalance in myocardial oxygen supply and demand related to noncoronary illness, such as stress of surgery or poorly controlled hypertension), because older patients constitute a large proportion of this population.
- Studies are needed to identify and implement optimal bleeding reduction strategies in older patients.*
- Studies are needed to understand delays in presentation among older adults and to develop strategies for reducing presentation and treatment delays, including education of family and caregivers.*

STABLE ISCHEMIC HEART DISEASE, PCI, AND CORONARY ARTERY BYPASS GRAFT SURGERY

Current Recommendations

The "2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guide line for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease" includes a section that focuses on management of patients with advanced age (section 5.12.2) (19). This section notes that older adults have a high prevalence of 3-vessel and left main disease and that ischemic heart disease (IHD) is a prominent source of morbidity and mortality. The guideline highlights the limitations of exercise stress testing in older patients and endorses pharmacological testing as a more useful option for diagnosis and prognosis in many older patients.

The guideline acknowledges that although there is strong rationale to treat IHD in older adults, there are limited data pertaining to older patients, and most recommendations are inferred from studies in younger

patients. Guideline-directed medical therapy is recommended as the initial approach for most patients with stable IHD, including the elderly. Revascularization is reasonable and appropriate in selected patients but should be undertaken only after due consideration of patient preferences, functional capacity, quality of life, and end-of-life issues (i.e., factors that often impact clinical decision making in older patients).

Current guidelines for PCI include a single paragraph devoted to older patients, in which it is noted that the number of patients ≥75 years of age undergoing PCI has increased markedly over the past 25 to 30 years (20). It is pointed out that older patients present with a substantially higher clinical risk profile than younger patients and that advanced age is one of the strongest predictors of mortality after PCI (21,22). Older patients are also at increased risk for major bleeding and stroke (23). However, despite increased risks, angiographic success rates and clinical benefits are similar in older and younger patients, and there is evidence that the absolute benefit may be greater in older patients because of higher baseline risk (24).

The "2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery" discusses issues pertaining to older adults in section 6.1 under "Specific Patient Subsets (25)." It is acknowledged that compared with younger people, patients ≥80 years of age undergoing coronary artery bypass graft surgery (CABG) are more likely to have greater extent and severity of coronary artery disease, left ventricular dysfunction, concomitant valve disease, and prior cardiac surgery. In addition, older patients are more likely to have comorbid lung disease, peripheral arterial disease, renal insufficiency, diabetes mellitus, and hypertension. Hematologic and hepatic disorders are also more prevalent and are not accounted for in the 2 most widely used cardiac surgical risk scoring systems: the Society of Thoracic Surgeons (STS) Predicted Risk of Mortality or Major Morbidity (STS-PROMM) (26,27) and the EuroSCORE II (28,29). The EuroSCORE II includes an assessment of poor mobility, defined as "severe impairment of mobility secondary to musculoskeletal or neurological dysfunction" that contributes to mortality. The most recent version of the STS score also incorporates gait speed as a surrogate for frailty. However, neither instrument adjusts for functional capacity or dementia, thus limiting their utility in patients ≥75 years of age.

As a result of increased cardiac and noncardiac morbidity, as well as age-associated declines in cardiac reserve and homeostasis, older patients are at increased risk for major perioperative complications, including stroke, cognitive dysfunction and delirium, renal failure, respiratory failure, and gastrointestinal disorders. The guideline highlights the marked increase in operative mortality that occurs in patients aged 75 to 79 years and those >80 years of age undergoing CABG (30,31). In studies published from 2000 to 2007, operative mortality was up to 2-fold higher in octogenarians, and the rate of discharge to home was half that of younger patients (32–34). Average intensive care unit and total hospital length of stay are also longer in older patients.

Recommendations to Close Knowledge Gaps

[Note: Recommendations marked with an asterisk (*) also apply to the section on ACS.]

- Research is needed to determine the impact of IHD on symptoms, activities of daily living, health status, and maintenance of independence in older adults. Improved recognition and management of symptoms has the potential to enhance function and quality of life for older adults with IHD.*
- Studies are needed to better define the role of pharmacological stress imaging in the diagnosis and management of stable IHD in older adults. Although imaging increases the sensitivity of ischemic assessment, overreliance on imaging may potentially lead to management that is dissociated from symptoms and patient preferences. Conversely, underutilization of imaging may lead to underdiagnosis and undertreatment, with the potential for detrimental effects on patient-centered outcomes.
- Studies are needed to assess the utility of alternative methods to traditional stress testing to assess symptoms and functional status in older patients, such as submaximal exercise tests, walk tests, gait speed, gait variability, cardiopulmonary indices, strength indices (e.g., hand grip), and mental stress indices, as metrics to guide IHD management.
- The comparative effectiveness of medical therapy versus early invasive management (including PCI and CABG), particularly with respect to quality of life, functional capacity, and medication use, warrants further investigation in older adults.
- Studies are needed to evaluate the potential role of physical conditioning before major procedures as a means for reducing periprocedural risk and improving postprocedural outcomes.
- Studies are needed to refine the utility of cardiac rehabilitation programs to optimize functional capacity, reduce disability and fall risk, preserve independence, decrease hospital and long-term care admissions, and lower healthcare costs in older patients with IHD.*
- Studies are also needed to improve referral and adherence to cardiac rehabilitation among older adults, including patients with multimorbidity, noncardiovascular functional limitations, and frailty.*

- Studies are needed to assess the effectiveness and comparative effectiveness of various antithrombotic regimens in older patients with or without relevant comorbidities (e.g., concomitant atrial fibrillation [AF], advanced renal insufficiency, or high risk for falls or bleeding).*
- Studies are needed to evaluate the importance of the patient's attitudes and psychological reserve (e.g., drive to recover/will to live) as factors that impact the likelihood of a favorable outcome after cardiac surgery (35).
- Studies are needed concerning how best to assess and incorporate advance care planning into the decision-making process before a major intervention is undertaken and whether early consideration of goals of care influences choice of therapy.*
- Additional studies are needed to develop methods for estimating procedural risks and potential benefits over various time horizons that can be used to facilitate shared decision making (e.g., what are the risks and benefits of medical therapy versus PCI versus CABG for treatment of chronic IHD in an 80-year-old patient with specific comorbid conditions over periods of 1, 2, and 5 years?).*
- Collaborative studies with neurologists, radiologists, geriatricians, and other disciplines are needed to develop novel imaging techniques, neurocognitive tests, biomarkers, and genetic markers for mild cognitive impairment and dementia and to determine domains of cognitive dysfunction most closely associated with procedural risks and postprocedural outcomes.*
- Studies are needed to identify patients at high risk for postoperative agitation and delirium and to develop strategies for preventing or minimizing and treating these conditions.

HEART RHYTHM DISORDERS

AF and Atrial Flutter

Current Recommendations

The "2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation" provides a brief subsection (7.2) on AF in the elderly (36). The authors note that ≈35% of patients with AF are >80 years of age. AF may occur in elderly patients without underlying heart disease because of "changes in cardiac structure and function that accompany aging, such as increased myocardial stiffness." The elderly are a heterogeneous group with potential for multiple comorbidities, and a Table listing the most common coexisting conditions in Medicare beneficiaries with AF is provided (36,37). Symptoms are frequently atypical among older patients, and palpitations are less common than in younger patients. In discussing medical management, the guideline cautions that older adults may be more prone to heart block, especially with use of amiodarone and digitalis. Increasing age is a potent risk factor for stroke in patients with AF, and this has been highlighted in the CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age ≥75, Diabetes mellitus, Stroke or transient ischemic attack, Vascular disease, Age 65-74, Sex category female) risk scoring system, which assigns 1 point for age 65 to 74 years and 2 points for age ≥75 years. Although most AF trials have enrolled patients without an upper age limit, the mean age of study cohorts is 5 to 10 years younger than the average age of patients with AF in the general population. Therefore, it is unknown whether the findings of these studies can be generalized to patients ≥75 years of age, and especially those ≥85 years of age.

TABLE Ten Most Common Chronic Comorbid Conditions Among Medicare Beneficiaries With Atrial Fibrillation (36)

Beneficiaries ≥65 y of Age (N = 2,426,865) (Mean Number of Conditions = 5.8; Median = 6)			Beneficiaries <65 y of Age (N = 105,878) (Mean Number of Conditions = 5.8; Median = 6)		
	N	%		N	%
Hypertension	2,015,235	83.0	Hypertension	85,908	81.1
Ischemic heart disease	1,549,125	63.8	Ischemic heart disease	68,289	64.5
Hyperlipidemia	1,507,395	62.1	Hyperlipidemia	64,153	60.6
HF	1,247,748	51.4	HF	62,764	59.3
Anemia	1,027,135	42.3	Diabetes mellitus	56,246	53.1
Arthritis	965,472	39.8	Anemia	48,252	45.6
Diabetes mellitus	885,443	36.5	CKD	42,637	40.3
CKD	784,631	32.3	Arthritis	34,949	33.0
COPD	561,826	23.2	Depression	34,900	33.0
Cataracts	546,421	22.5	COPD	33,218	31.4

Reproduced from the Centers for Medicare & Medicaid Services (37).

AF indicates atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; and HF, heart failure.

In the most recent consensus statement on AF ablation (38), and in the 2014 guideline (36), it is acknowledged that older patients are not well represented in the ablation literature. Data on long-term outcomes after ablation in the older population are lacking. Atrioventricular node ablation to create complete heart block with pacemaker implantation to maintain a regular rhythm in patients for whom pharmacological therapy has failed carries a Class IIa recommendation as an alternative nonpharmacological approach to management of patients with symptomatic AF without specific reference to age (36,39,40).

Recommendations to Close Knowledge Gaps

- Studies are needed to better understand mechanisms underlying interactions between common diseases (coronary artery disease, hypertension, diabetes mellitus, heart failure (HF), obstructive sleep apnea, obesity) and age-mediated changes in atrial structure, function, biochemistry, and biophysics that increase the propensity to develop AF with increasing age.
- Noninvasive tools are needed to study and quantify aging-related structural and electrophysiological changes and remodeling that promote AF.
- Novel biomarkers or monitoring devices aimed at primary prevention or early detection of AF in the older population should be sought, because many strokes occur in patients with subclinical AF (41,42).
- Mechanisms that explain racial variations in AF prevalence with advancing age (e.g., less common among older blacks despite higher prevalence of risk factors) should be sought, because these may provide insights into pathophysiology.
- Studies are needed to refine predictive models for both thromboembolic and bleeding complications in older adult patients with AF. In addition to clinical characteristics, including the impact of multimorbidity and frailty, structural factors and biological and genetic markers warrant further investigation.
- The value of novel point-of-care calculators (e.g., the Stroke Prevention in Atrial Fibrillation Risk Tool [43]) for estimating benefits and bleeding risks associated with antithrombotic therapy and as an aid to clinical decision making in older adults with AF should be tested.
- Comparative effectiveness studies, large registries, and mandatory postmarketing surveillance databases are needed to define specific clinical situations in which one anticoagulant offers a superior benefit-to-risk profile relative to other available treatments.
- Studies are also needed to determine the consequences of nonadherence with anticoagulation therapy, as well as whether risks of adverse events differ across current and emerging anticoagulant agents.
- Additional studies of nonpharmacological approaches to stroke prevention, such as procedures that occlude or ligate the left atrium, are needed in older populations.
- Studies are needed to define criteria for withholding and withdrawing anticoagulants in older patients (e.g., because of terminal illness or excessive risking of bleeding).
- Studies are needed to test the differences between rate and rhythm control strategies on clinical outcomes relevant to older populations, such as quality of life and functional status.
- Risks and benefits of AF ablation should be studied in older populations with respect to short- and long-term outcomes, including quality of life and healthcare costs.
- Studies are needed to determine the appropriate use of anticoagulation therapy after successful AF ablation.
- Studies are needed to assess the impact of atrioventricular node ablation with pacemaker implantation on quality of life and other relevant outcomes in older patients with AF.

VENTRICULAR ARRHYTHMIAS AND PREVENTION OF SUDDEN CARDIAC DEATH

Current Recommendations

The "ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" include a section devoted to the management of older adults (44). The guidelines note that although the incidence of ventricular arrhythmias increases with age, there appears to be a decline in sudden cardiac death after age 80 years because of competing causes of death. In general, medical therapy for ventricular arrhythmias does not differ by age, but dosage adjustment because of alterations in renal and hepatic clearance and changes in volume of distribution must be considered. The guidelines do not discuss catheter ablation, surgical interventions, or revascularization as secondary prevention strategies for ventricular arrhythmias in older adults.

Recommendations to Close Knowledge Gaps

- Improved noninvasive risk stratification tools are needed to identify older adults at increased risk of sudden cardiac death. Screening tools should be applicable to a broad spectrum of older adults, including those with functional and cognitive limitations.
- Studies of prevention of sudden cardiac death should include quality-of-life end points and quality-adjusted life-years added, because these outcomes may be of particular concern to older adults.

- Studies are needed to understand the role of catheter ablation of ventricular arrhythmias in older adults.
- Studies of competing risks should be performed to assess the relative risk of death caused by arrhythmias compared with death from other causes.
- Point-of-care resources are needed to assist healthcare providers in appropriately dosing antiarrhythmic drugs in older adults, including consideration of drug interactions and age-related alterations in pharmacokinetics.

DEVICE-BASED THERAPY FOR CARDIAC RHYTHM ABNORMALITIES

Current Recommendations

Both the "ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" and "ACC/AHA/HRS 2008 Guidelines for Device-based Therapy of Cardiac Rhythm Abnormalities" have sections devoted to older adults (44,45). The 2006 guidelines note that "comorbidities, life expectancy, and quality-of-life issues must be addressed forthrightly with patients and their families (44)." The guidelines specifically state that a device should not be placed in a person with a life expectancy <1 year.

Class I indications for pacemaker implantation and for cardiac resynchronization therapy are similar in older and younger patients (46,47). The 2012 guideline update supports remote monitoring after the initial 2-week period (46). This is of particular importance to older adults, some of whom may have physical limitations that make frequent in-person visits more challenging. However, patients with cognitive impairment may have difficulty performing home-based transmissions. Remote monitoring may also allow for earlier detection of clinical deterioration, thereby leading to reduced readmission rates.

Although the guidelines for implantable cardioverter-defibrillators (ICDs) do not distinguish indications based on age, it is acknowledged that "few clinical trials of device-based therapy have enrolled enough older patients to reliably estimate the benefits of device-based therapy in this group (44)." The durability of ICD benefit is shorter and the risk of procedural complications is higher in patients >80 years of age than in younger patients (48). Thus, the guideline states that older patients with limited life expectancy may not be suitable candidates for an ICD. Conversely, it is noted that many older patients who die suddenly are fully functional during the month before death (49).

There is a specific section of the guidelines for device-based therapy that addresses end-of-life planning in patients with cardiac devices, stating that such devices should not be placed in those with life expectancy <1 year (50). "These decisions require not only evidence of clinical benefit demonstrated in randomized clinical trials but also estimates of life expectancy, consideration of comorbidities and procedural risk, and patient preferences. Although these factors are important when device implantation is considered in any age group, they assume greater weight in clinical decision making among the elderly (45)."

The guidelines also have a section on device deactivation. Clinicians who implant devices are encouraged to discuss end-of-life issues before implantation. If a decision is made to deactivate the device, the conversation should be documented in the record, a do-not-resuscitate order should be placed, and a psychiatry or ethics consultation should be obtained if appropriate (51). The guidelines opine that "age itself should not be the predominant consideration in the use of device-based therapy among the elderly."

Recommendations to Close Knowledge Gaps

- More research is needed on mechanisms of degeneration of the cardiac conduction system with increasing age. The potential for conduction cell regeneration (e.g., stem cell therapy to treat sinus node dysfunction) in older adults should be explored.
- Better methods are needed for identification of older adults with unexplained syncope who have bradyarrhythmias as the underlying cause (e.g., arrhythmia detection patches or implantable loop recorders).
- Studies are needed to determine the impact of cardiac resynchronization therapy, with or without defibrillation, on clinical outcomes, including quality of life and functional status, in older adults.
- Studies to improve management of implanted cardiac devices at the end of life with regard to device disablement and cost-benefit issues are needed.
- Data are needed on outcomes of ICD implantation for primary and secondary prevention of sudden cardiac death in a broad spectrum of older adults, including procedural complications, quality-adjusted life-years gained, and healthcare costs.
- Individualized ICD consent forms need to be developed that estimate the anticipated life extension associated with implantation while accounting for prevalent comorbidities.
- Studies are needed on decision making at the time of generator replacement for battery end of life. Cohort studies to evaluate outcomes of older adults in this setting could provide important insights into the continued need for such devices.

VALVULAR HEART DISEASE: AORTIC STENOSIS

Current Recommendations

The "2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease" section on aortic stenosis (AS) is largely based on data from studies in older adults; therefore, the discussion and recommendations in this section are generally applicable to older adults (52). The guideline notes that compared with younger patients, symptoms among older patients are both less sensitive and less specific for AS. Similarly, classic physical findings of AS, such as delayed carotid upstroke, are less common in older adults, in part because of age-related changes in the vasculature (53). Disease progression may also vary in relation to age and sex and tends to be more rapid in older patients (54,55).

The guideline emphasizes that age is not a contraindication to aortic valve replacement (AVR) (52), with several series showing excellent outcomes in very elderly patients undergoing surgical or transcatheter AVR (TAVR) (56–59). The guideline recommends determining the operative risk for each individual using an online calculator such as that of the STS (www.sts.org) (60). It is noted that concomitant diseases (e.g., permanent neurological defects or cancer) and severe debilitation have a major impact on outcomes and may make AVR inappropriate. In this regard, the guideline provides a Class III recommendation for TAVR in patients in whom existing comorbidities would preclude the expected benefit from correction of AS (Level of Evidence: B). The guideline also states that AVR is not indicated in patients with a life expectancy <1 year or with a likelihood of 2-year survival with benefit <25%. In the PARTNER studies (Placement of Aortic Transcatheter Valves), patients with an STS score ≥15, frailty, porcelain aorta, or prior chest radiation were less likely to benefit from TAVR than those without these features (58,61).

The guideline acknowledges the important role of patient preferences in the decision-making process and points out that a multidisciplinary heart valve team may be particularly beneficial in evaluating older patients for possible AVR. In addition, it is noted that certain anatomic factors more common in older adults, such as a narrow left ventricular outflow tract or heavily calcified aortic annulus, may render surgery more challenging in this population.

Recommendations to Close Knowledge Gaps

- Basic and translational studies examining the mechanisms of inflammation and calcification of the aortic valve that lead to the development and progression of AS are essential.
- Interactions between age, sex, race/ethnicity, and comorbidities (e.g., hypertension, diabetes mellitus, coronary artery disease, and obesity) with the clinical course and prognosis of older adults with AS should be explored.
- Risk calculators should be developed that include cognitive function, frailty, and functional limitations in the assessment of perioperative morbidity and mortality, as well as long-term outcomes, including functional status and quality of life.
- The potential role of medical therapies in slowing the rate of disease progression and reducing symptoms remains to be established; in addition, the risk versus benefit of any such medications in relation to advanced age, frailty, and comorbidity requires elucidation.
- The role of percutaneous balloon aortic valvuloplasty in selected older adults with severe AS in the era of TAVR remains uncertain and warrants further study.
- Novel techniques are needed to reduce periprocedural complications (e.g., stroke, paravalvular aortic regurgitation, heart block, AF, and cognitive impairment/delirium) and to expedite recovery with return to independent living.
- Further studies are needed to determine the role of TAVR in intermediate-risk older adults, in those with predominant aortic regurgitation, and in those with bioprosthetic valve failure.
- Improved methodologies and criteria are needed to refine patient selection to identify patients most likely to benefit from surgical AVR, TAVR, or conservative management (e.g., expected survival <1 year even with successful intervention).
- Further studies are needed to define the pathogenesis and mechanisms of paradoxically low-flow AS, which disproportionately afflicts older adults, as well as the outcomes of such patients with interventional approaches.
- Additional studies are needed to evaluate the impact of pulmonary hypertension, which is common in older patients, on clinical and functional outcomes after AVR.

HEART FAILURE

Current Recommendations

HF With Reduced Ejection Fraction

The "2013 ACCF/AHA Guideline for the Management of Heart Failure" focuses mainly on the evaluation and management of patients with HF and reduced ejection fraction (HFrEF) (47). The guideline emphasizes the strong and consistent association of advancing age with the prevalence and incidence of HF, noting that HF is predominantly a disease of older adults and that with the aging of the population, the number of Americans with HF is expected to increase significantly (62). The guideline

also notes that in older adults, HF is inadequately recognized and treated, often because symptoms are incorrectly attributed to normal aging or other conditions.

Throughout the guideline, special issues pertinent to older adults are highlighted, including the following: the observation that 3% to 4% of blacks carry an allele of the serum protein transthyretin (TTR V122I) that appears to increase risk for cardiac amyloid deposition and HF after 65 years of age; the risk of hyperkalemia with standard pharmacological therapy for HF and the underestimation of renal dysfunction in older adults based on serum creatinine; the association of advancing age with increases in natriuretic peptides, thereby limiting their diagnostic utility and their usefulness in guiding therapy in older adults; uncertainty about the value of revascularization in patients with HF and coronary artery disease but without angina; the increased risk of digoxin toxicity in older adults because of impaired renal function and lower lean body mass; and the stronger association of AF to HF with advancing age. The guideline acknowledges that older adults with HF typically have multimorbidity (75% of HF patients >65 years of age have multiple chronic conditions) and that there is therefore a need to consider comorbid conditions, life expectancy, and personal preferences in the application of medical and device therapies. On the basis of data in younger patients, the guideline suggests that such therapies be used in older patients without an age limit but that treatment be individualized based on each patient's unique circumstances and goals of care.

There is growing interest in mechanical circulatory support (MCS) as destination therapy for older adults with advanced HFrEF, especially patients more than 70 to 75 years old who are not considered candidates for heart transplantation in most centers. The HF guideline and AHA statement on the use of MCS (63) indicate that the decision to use MCS as destination therapy requires a careful evaluation by an expert multidisciplinary team. Advanced age is a risk factor for adverse outcomes, and age ≥80 years is considered a relative contraindication to destination therapy- MCS. Optimal patient selection for MCS is an area of active investigation. Notably, Centers for Medicare & Medicaid Services guidelines for MCS require inclusion of a palliative care specialist on the multidisciplinary team.

Comprehensive discharge planning and postdischarge support with special attention to care transitions should be deployed to achieve guideline-directed medical therapy and prevent hospitalizations, which may in turn improve quality of life and survival without increasing costs. Recognizing that HF is a progressive and incurable disorder, the guideline endorses palliative care as an ongoing component of management, especially for patients hospitalized with recurrent decompensation. Palliative care should include early, regular discussions of prognosis with patients and families; the formulation and implementation of advance directives; ensuring appropriate transitional care across venues (home, emergency department, hospital, skilled nursing facility, hospice); discussions regarding devices and the option of defibrillator deactivation; and optimal relief of symptoms (Class I, Level of Evidence: B) (64,65).

HF With Preserved Ejection Fraction

In contrast to the sections devoted to HFrEF, the section of the 2013 HF guideline devoted to HF with preserved ejection fraction (HFpEF) is brief (47). Although the guideline acknowledges that HFpEF accounts for up to 50% of HF in the community and that it is predominantly a disorder of older women with hypertension, often in combination with other comorbidities (e.g., obesity, coronary artery disease, diabetes mellitus, AF) (66), the guideline does not provide recommendations for management of HFpEF because of the inadequacy of the existing evidence base.

The guideline defines diagnostic criteria for HFpEF as signs and symptoms of HF, a normal or near-normal left ventricular ejection fraction, and no other obvious explanation for the patient's symptoms. This simplified, phenomenological approach, without mandate for documentation of diastolic dysfunction or elevated natriuretic peptide levels, is supported by recent studies.

The guideline notes that there are currently no proven effective therapies for HFpEF. All completed clinical trials in HFpEF have been neutral for their primary outcomes. The guideline emphasizes the need for additional research to better define the pathophysiology and treatment of this disorder.

As a consequence of the limited evidence base, treatment recommendations are sparse, largely empiric, and focus on a few general principles: control of hypertension, judicious use of diuretic agents for pulmonary congestion and peripheral edema, control of AF, and treatment of myocardial ischemia in selected patients.

Recommendations to Close Knowledge Gaps

- Pooled data from high-quality clinical trials and large prospective registries should be scrutinized to inform clinicians about the impact of specific drug and device therapies, as well as exercise training and other lifestyle interventions, on relevant outcomes in older adults with HFrEF (67).
- Data are needed in older patients with left ventricular ejection fractions of 40% to 55% to determine whether pharmacological therapies improve mortality, hospitalizations, quality of life, or functional capacity in this poorly studied population.

- Studies are needed to determine the value of MCS as destination therapy in older patients with HFrEF, including complication rates, and the impact on quality of life, quality-adjusted life-years, caregiver burden, and healthcare use and costs, as well as whether age-related disorders in cognitive function (including mild cognitive impairment) and frailty are potentially reversible with MCS.
- Studies are needed to better characterize the bidirectional association between HF and cognitive impairment in older adults, evaluate cognitive outcomes in older HF patients, and develop and test interventions that may slow progression of cognitive decline.
- Similarly, studies are needed to further evaluate the impact of depressive symptoms on clinical outcomes and response to therapy in older patients with HF, better understand the intersections between depression and cognitive dysfunction in this population, and develop interventions for these overlapping syndromes.
- Studies are needed to better understand the processes of symptom recognition and the decision to seek treatment in older adults with HF.
- Strategies are needed to ensure optimal care transitions across venues (hospital, skilled nursing facility, emergency department, home) among older HF patients (68).
- Early and more systematic introduction of palliative care services for older adults with HF, including consideration for hospice care if appropriate, by use of a process of shared decision making is needed to better align patient and family preferences with therapeutic choices for advanced HF care.
- Research is needed on behavioral approaches to managing both acute and chronic HF in patients with either HFrEF or HFpEF. Studies should evaluate dietary and exercise interventions, alone and in combination, and determine their impact on quality of life, functional capacity, body composition, preservation of independence, and clinical events.
- Studies are needed to evaluate specific dietary patterns (e.g., sodium and potassium intake, fluid intake), as well as the role of dietary supplements (e.g., coenzyme Q10, vitamin D) in older patients with HFrEF or HFpEF and whether optimal intake of these and other nutrients varies as a function of age, renal function, and hepatic function.
- Better understanding of the mechanisms culminating in HFpEF is needed, with the recognition that there is substantial heterogeneity of HFpEF in the older population, that mechanisms of HFpEF likely vary across individuals, and that there is a marked sexual dimorphism.
- More data are needed on peripheral abnormalities, such as arterial and skeletal muscle dysfunction, which appear to be major contributors to exercise intolerance in HFpEF. Therapies that target these abnormalities warrant further investigation, particularly because skeletal muscle has robust capacity for rapid regeneration and remodeling.
- Studies that consider HFpEF as a marker for loss of global reserve capacity in multiple organ systems and as a systemic disorder, rather than merely as an isolated cardiac or vascular abnormality (e.g., myocardial stiffness), could lead to significant advances in prevention and management.

PERIPHERAL ARTERIAL DISEASE

Current Recommendations

The "ACC/AHA 2005 Practice Guidelines for the Management of Patients With Peripheral Arterial Disease" and the "2011 ACCF/AHA Focused Update" address the diagnosis and treatment of peripheral arterial disease (PAD) in 4 extracardiac vascular beds (abdominal aorta, renal and mesenteric arteries, and the lower limb arteries) (69,70). The guidelines highlight the strong and consistent association of advancing age with the prevalence and incidence of PAD. Age >70 years is noted to be an independent risk factor for the development of PAD involving the lower extremities, irrespective of other risk factors, with prevalence rates of >20% in both men and women in this age group. Given the strong effect of age on PAD prevalence, the guidelines endorse as a Class I (Level of Evidence: C) recommendation that providers inquire in adults ≥50 years of age about a family history of abdominal aortic aneurysm among first-degree relatives to identify high-risk individuals who may require additional evaluation. For older adults who may have noncompressible arteries because of calcification, caution is advised about limitations of the ankle brachial index for diagnosing PAD and the potential for false-negative results. Recognizing that many older adults are not able to exercise on a treadmill because of comorbid conditions, the guidelines recommend the use of hall walks for evaluation of functional capacity and to assess response to therapy and prognosis. There is also recognition that consideration of life expectancy is essential for development of patient-centered treatment recommendations for the management of PAD, a point that is especially relevant to older adults who may have competing causes for future morbidity and mortality.

Recommendations to Close Knowledge Gaps

- Comparative effectiveness studies are needed in patients with PAD who are >75 years of age and are treated with medical, surgical, or percutaneous interventions.

- Studies are needed on the impact of PAD on quality of life and functional outcomes, including absence of disability (e.g., performance of activities of daily living), mobility, gait speed, and independence in older adults.
- Studies are needed to assess the utility of pharmacological therapies (antiplatelet agents, lipid-lowering drugs, anticoagulant agents, phosphodiesterase inhibitors, and others) in the context of competing conditions (an average of ≥3 comorbidities) (71) in older adults with PAD.
- To identify new targets for pharmacological therapy, research that delineates the biological mechanisms underlying the propensity of older adults to develop PAD is warranted.
- The intersection of PAD with age-related declines in skeletal muscle mass and function (sarcopenia) (71) that contribute to the development of functional impairments (e.g., gait speed) and subsequent disability warrants further investigation, with emphasis on interventions that could optimize functional outcomes and quality of life.
- Research is needed on the use of exercise interventions to optimize function and decrease disease progression, especially the type, amount, and intensity of activity required to achieve benefit in the oldest old (i.e., patients ≥85 years of age).
- Studies are needed to determine the predictive value of impaired functional capacity attributable to PAD and the impact of interventional therapies for the prevention of critical limb ischemia and limb loss.

CEREBROVASCULAR DISEASE AND STROKE

Current Recommendations

Cerebrovascular disease and stroke comprise several discrete and heterogeneous conditions, mostly affecting elderly patients. Since 2010, there have been at least 11 ASA/AHA guidelines and scientific statements related to cerebrovascular disease and stroke (72–82). Common themes are that older adults tend to have more complex anatomy and greater vessel tortuosity and that older adults are at increased risk for adverse outcomes from stroke (higher likelihood of hemorrhagic transformation, reduced neurological recovery, and increased mortality), as well as from pharmacological, percutaneous, and surgical interventions. It is also acknowledged that older patients and women have been underrepresented in clinical trials and that additional research is needed to better define optimal prevention and treatment for cerebrovascular disease and stroke in these populations.

The 2014 scientific statement on "Palliative and End-of-Life Care in Stroke" from the AHA/ASA promotes a focus on "patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering," while also recommending a balanced and collaborative approach to end-of-life decision making. These issues cut across all types of stroke and are especially important in elderly stroke patients (80). Recommendations and comments specific to elderly patients include the following:

- For chronic poststroke pain, pharmacological treatment with amitriptyline or lamotrigine is reasonable, although in older adults, given the side effects associated with amitriptyline, nortriptyline may be a reasonable substitute (Class IIa; Level of Evidence: B).
- In vulnerable populations (older adults and those with impaired communication), there should be enhanced strategies for detection and monitoring of symptoms, including pain, "including verbal descriptor scales, caregiver report, and knowledge of pain behaviors (75)."

Ischemic stroke is by far the most common type of stroke in the United States and is covered in 8 of the 11 recent guidelines, although none have sections specifically devoted to the elderly (73,74,77–82). There are a number of recommendations and comments related to the care of elderly patients with acute ischemic stroke:

- The effectiveness of intravenous treatment with recombinant tissue plasminogen activator is not well established (Class IIb; Level of Evidence: C) and requires further study for patients who can be treated in the time period of 3 to 4.5 hours after stroke but have ≥1 of the following exclusion criteria: 1) patients >80 years old, 2) those taking oral anticoagulants, even with international normalized ratio ≤1.7, 3) those with a baseline National Institutes of Health Stroke Scale score >25, or 4) those with a history of both stroke and diabetes mellitus (78).
- Decompressive surgery for malignant edema of the cerebral hemisphere is effective and potentially lifesaving (Class I; Level of Evidence: B). Advanced patient age and patient/family valuations of achievable outcome states may affect decisions regarding surgery (78).
- The efficacy of decompressive craniectomy in patients >60 years of age and the optimal timing of surgery are uncertain (Class IIb; Level of Evidence: C) (82).
- The value of surgery for elderly patients with massive cerebellar lesions (ischemic or hemorrhagic) and severe comorbidities has never been examined formally; in these cases, the decision to proceed with surgery needs to be individualized with consideration of the overall prognosis for recovery and the patient's wishes (80).

Intravenous tissue plasminogen activator remains somewhat controversial in ischemic stroke patients

>80 years old, although the Third International Stroke Trial (IST-3) suggested that the benefit of tissue plasminogen activator was at least as great in patients ≥80 years of age as in younger patients (83). In 2014, the DESTINY II study (Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery II) reported results of a randomized trial of decompressive hemicraniectomy versus conservative management in patients ≥61 years of age (median age 70 years) with large middle cerebral artery ischemic stroke. Although there were significantly more patients "without severe disability" (modified Rankin Scale score ≤4) in the hemicraniectomy group, the majority of these patients were still dependent for most activities of daily living (84).

Multiple guidelines and statements raise age-specific issues for primary stroke prevention, including the following:

- Aggressive management of blood pressure coupled with antithrombotic prophylaxis in elderly patients with AF can be useful (Class IIa; Level of Evidence: B) (74).
- Across the spectrum of age groups, including adults >80 years of age, the benefit of hypertension treatment in preventing stroke is clear (74).
- The benefits versus risks of the combined use of antiplatelet agents in addition to warfarin in elderly AF patients are inadequately defined (74).
- Given the increased prevalence of AF with age and the higher risk of stroke in elderly women with AF, active screening (in particular of women >75 years of age) in primary care settings using pulse taking followed by an electrocardiogram as appropriate is recommended (Class I; Level of Evidence: B) (79).
- Carotid duplex ultrasound screening is reasonable before elective CABG surgery in patients >65 years of age and in those with left main coronary stenosis, PAD, a history of cigarette smoking, a history of stroke or transient ischemic attack, or carotid bruit (Class IIa; Level of Evidence: C) (73).

Secondary ischemic stroke prevention recommendations focused on the elderly include the following:

- Apixaban 5 mg twice daily is a relatively safe and efficacious alternative to warfarin or aspirin in patients with nonvalvular AF deemed appropriate for vitamin K antagonist therapy who have at least 1 additional risk factor and no more than 1 of the following characteristics: age ≥80 years, weight ≤60 kg, or serum creatinine ≥1.5 mg/dL (Class I; Level of Evidence: B) (77).
- Although its safety and efficacy have not been established, apixaban 2.5 mg twice daily may be considered as an alternative to warfarin or aspirin in patients with nonvalvular AF deemed unsuitable for vitamin K antagonist therapy who have at least 1 additional risk factor and ≥2 of the following criteria: age ≥80 years, weight ≤60 kg, or serum creatinine ≥1.5 mg/dL (Class IIb; Level of Evidence: C) (77).
- The decision to restart antithrombotic therapy after intracerebral hemorrhage (ICH) related to antithrombotic therapy depends on the risk of subsequent arterial or venous thromboembolism, the risk of recurrent ICH, and the overall status of the patient and must therefore be individualized. For patients with a comparatively lower risk of cerebral infarction (e.g., AF without prior ischemic stroke) and a higher risk of recurrent ICH (e.g., elderly patients with lobar ICH or presumed amyloid angiopathy) or with very poor overall neurological function, an antiplatelet agent may be considered for prevention of ischemic stroke (Class IIb; Level of Evidence: B) (81).
- It is reasonable to consider patient age in choosing between carotid artery stenting and carotid endarterectomy. For patients >70 years of age, carotid endarterectomy may be associated with improved outcome compared with carotid artery stenting, particularly when arterial anatomy is unfavorable for endovascular intervention. For younger patients, carotid artery stenting is equivalent to carotid endarterectomy in terms of risk for periprocedural complications (i.e., stroke, myocardial infarction, or death) and long-term risk for ipsilateral stroke (Class IIa; Level of Evidence: B) (81).

ICH is the most lethal form of stroke, especially in the elderly. One recommendation from the 2010 "Guidelines for the Management of Spontaneous Intracerebral Hemorrhage" (72) makes reference to older age:

- In situations where stratifying a patient's risk of recurrent ICH may affect other management decisions, it is reasonable to consider the following risk factors for recurrence: lobar location of the initial ICH, older age, ongoing anticoagulation, presence of the apolipoprotein ε2 or ε4 alleles, and greater number of microbleeds on magnetic resonance imaging (Class IIa; Level of Evidence: B).

Recently, the 2013 report of the STICH II trial (Surgical Trial in Lobar Intracerebral Hemorrhage; ≈40% ≥70 years of age) suggested the possible benefit of early surgical intervention, specifically for superficial ICHs. The benefit of early surgery in superficial ICHs may be accentuated in patients with a poor prognosis, with older age being a prominent risk factor for poor prognosis (85).

Prognostic models for ICH outcomes may be overly pessimistic because of biases introduced by the inclusion of patients managed with comfort measures only or

withdrawal of life support. Thus, there is a recommendation for aggressive full care early after ICH onset and postponement of new do-not-resuscitate orders until at least the second full day of hospitalization to better allow time for appropriate family counseling and decision making (Class IIa; Level of Evidence: B) (72). However, this recommendation may not be as relevant for older patients, especially those with severe hemorrhages, who more commonly have significant medical comorbidities and preestablished end-of-life care plans (72).

Subarachnoid hemorrhage is most commonly caused by rupture of an intracranial aneurysm. The 2012 "Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage" include 1 recommendation and 1 comment related to the elderly (76):

- Microsurgical clipping may receive increased consideration in patients presenting with large (>50 mL) intraparenchymal hematomas and middle cerebral artery aneurysms. Endovascular coiling may receive increased consideration in the elderly (>70 years of age), in those presenting with poor-grade (World Federation of Neurological Surgeons classification IV/V) subarachnoid hemorrhage, and in those with aneurysms of the basilar apex (Class IIb; Level of Evidence: C).
- In older patients with degenerative vascular diseases, computed tomographic angiography can replace catheter cerebral angiography in most cases if the image quality is excellent and analysis is performed carefully.

A comment from the 2014 "Palliative and End-of-Life Care in Stroke" statement cautions that "although elderly, comatose patients with poor-grade SAH [subarachnoid hemorrhage] have a high likelihood of a poor outcome, it still may be reasonable to attempt a limited trial of aggressive treatment for some patients given the potential for considerable recovery (80)."

Vascular cognitive impairment is primarily a condition of the elderly and is caused by clinical strokes, silent strokes, and white matter lesions. It is the second most common cause of dementia and overlaps with Alzheimer disease in a substantial proportion of patients. The entire statement "Vascular Contributions to Cognitive Impairment and Dementia" focuses on the role of cerebrovascular pathology and the development of late-life dementia, and thus, the elderly (75). Recommendations specifically pertaining to the elderly include the following:

- There is reasonable evidence that in the middle-aged and young-elderly, lowering blood pressure can be useful for the prevention of late-life dementia (Class IIa; Level of Evidence: B).
- The usefulness of lowering blood pressure in people >80 years of age for the prevention of dementia is not well established (Class IIb; Level of Evidence: B).

Recommendations to Close Knowledge Gaps

- Comparative effectiveness studies are needed to assess short- and long-term outcomes in elderly patients with all stroke types and to define which patients are most likely to benefit from specific interventions.
- Additional research is needed to identify the best approaches to help families understand the range of possible functional outcomes in elderly patients with severe stroke and to use that information to make individualized decisions about continued aggressive care based on their understanding of the patient's wishes.
- Studies are needed to establish optimal blood pressure targets and intensity of statin therapy for primary and secondary stroke prevention in older adults.
- The role of thrombolysis for acute ischemic stroke in the elderly requires further clarity.
- Further research is needed to better understand which elderly patients benefit from carotid interventions, why elderly patients appear to fare better with carotid endarterectomy, and whether management of their care should differ from that for younger patients (73).
- Additional large-scale magnetic resonance imaging studies of cerebral microhemorrhages as predictors of cerebral macrohemorrhages may prove to be useful in relation to the safety of administration of antithrombotic agents, especially in the elderly (74).
- Research is needed to develop and test novel less invasive approaches to ICH decompression for older patients.
- Additional research should better define the risk-benefit ratio of various antithrombotic therapies for the elderly who have competing risks of ischemic and hemorrhagic stroke.
- Studies are needed to better understand the relationship between location, severity, and extent of vascular brain injury and the resultant cognitive syndromes, while simultaneously accounting for coexisting age-related pathologies and cognitive reserve. These programs should include a search for genetic and other novel factors with an overarching goal to identify new strategies for prevention or treatment of vascular cognitive impairment (75).

PERIOPERATIVE MANAGEMENT FOR NONCARDIAC SURGERY

Current Recommendations

Older adults account for the majority of major surgical procedures performed in the United States and Europe, and it is estimated that the rate of surgery is up to 4-fold higher in older adults than in younger people (86). In addition, because the prevalence of CVD increases

progressively with age, the probability that an adult undergoing surgery has CVD (asymptomatic or symptomatic) also rises rapidly with age. Numerous studies have shown that advanced age (e.g., ≥80 years) is an independent predictor of perioperative complications and death after both cardiac and noncardiac surgery (87,88). Furthermore, older adults undergoing major surgery are at heightened risk for a host of noncardiac complications, including infections, pulmonary disorders (e.g., prolonged requirement for mechanical ventilation), renal insufficiency, postoperative cognitive impairment and delirium, gastrointestinal problems (e.g., anorexia, ileus), deep venous thrombosis and pulmonary embolism, dermatologic problems (e.g., pressure ulcers), and deconditioning (89). Taken together, these complications result in increased length of stay, increased likelihood of discharge to a transitional care or chronic care facility, increased risk for disability and dependency, reduced quality of life, and diminished likelihood of full recovery to preoperative levels of physical and mental function.

The "2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery" acknowledges that older adults are at increased risk for perioperative cardiac complications and death (86). The guideline recommends the use of validated prediction tools for assessing risk of perioperative major adverse cardiac events (90,91). In addition to age and functional status, sex is considered in the American College of Surgeons NSQIP (National Surgical Quality Improvement Program) Surgical Risk Calculator (90). However, although the guideline recognizes the impact of advanced age and functional limitations on surgical risk, it does not consider other geriatric issues, such as cognitive function, frailty, and multimorbidity, in risk assessment, and it does not include recommendations specific to the geriatric population (86).

Recommendations to Close Knowledge Gaps

- Studies are needed to develop methods to incorporate global risk (including, for example, multimorbidity, cognitive function, and frailty) and long-term outcomes relevant to older adults, such as maintenance of independence, preservation of physical and mental function, and overall quality of life, into preoperative cardiovascular risk assessment.
- Similarly, tools are needed to more accurately assess global risk in older patients referred for major cardiac and noncardiac surgical procedures, especially those ≥80 years of age and those ≥90 years of age, because data in these populations are sparse.
- Studies are needed to compare surgical risk calculators with respect to prediction of perioperative and long-term outcomes relevant to older adults.
- Additional studies are needed to better define what preoperative, perioperative, and postoperative tests and interventions are most efficacious in reducing cardiovascular risk in older patients undergoing cardiac and noncardiac surgery.
- Additional research is also needed to better define the significance and optimal management of small postoperative elevations of troponin, especially given the increasing use of high-sensitivity troponin assays.
- Research is needed to develop strategies to define and incorporate patient preferences and goals of care into the decision-making process in older patients before major surgical procedures.
- Interventions are needed to reduce the risk of common complications (e.g., delirium, functional decline, disability, renal insufficiency, pneumonia and other infections) and enhance functional outcomes in older patients undergoing major surgery.
- Comparative effectiveness studies are needed to evaluate outcomes with conservative management versus treatment in older patients with nonemergent conditions.

SUMMARY

Despite the high prevalence of CVD in older adults, there is limited evidence to guide clinical decision making in patients >75 to 80 years of age, and virtually no high-quality evidence in patients >80 years of age with multiple coexisting conditions, major physical or cognitive disabilities, frailty, or residence in long-term care facilities. Moreover, there is little guidance for how to manage CVD and related interventions at the end of life. There is also a pervasive lack of information on the impact of diagnostic and therapeutic interventions on patient-centered outcomes in older adults, including quality of life, functional outcomes (e.g., ability to perform routine activities of daily living and instrumental activities of daily living), and maintenance of independence. Often there is an overemphasis on pharmacological and surgical or catheter-based interventions, with much less attention given to nonpharmacological interventions such as diet, lifestyle, and exercise. Care of older adults is also impacted by age-associated alterations in physiology of the cardiovascular system and other organ systems, as well as by mounting chronic comorbidities and disabilities. Although older patients with CVD are at increased risk for adverse outcomes, including death, such that the absolute benefit of effective therapeutic interventions is potentially greater than in younger patients, older patients are also at increased risk for complications arising from both pharmacological agents and diagnostic and therapeutic procedures. Thus, there is a fundamental shift in the balance of risk and benefit in older patients

that has been inadequately addressed in clinical trials and that must be considered on an individualized basis. The present scientific statement summarizes vital knowledge and evidence gaps relevant to common cardiovascular disorders with high prevalence in older adults. To overcome these deficiencies, there is a critical need for a multitude of large population-based studies and clinical trials using novel study designs that incorporate patient-centered outcomes relevant to older patients and, most importantly, that include a broad mix of older patients typical of those seen in clinical practice. The results of these studies will enable translation of key findings into future evidence-based guidelines, thereby transforming care and enhancing outcomes for the growing population of older people with CVD in the United States and around the world.

APPENDIX: LIST OF ACC/AHA/ASA GUIDELINES REVIEWED

- 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction (12)
- 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes (16)
- 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease (19)
- 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention (20)
- 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery (25)
- 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation (36)
- ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death (44)
- 2012 ACCF/AHA/HRS Focused Update Incorporated Into the ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities (46)
- 2013 ACCF/AHA Guideline for the Management of Heart Failure (47)
- 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease (52)
- 2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Peripheral Artery Disease (70)
- Guidelines for the Management of Spontaneous Intra cerebral Hemorrhage (2010) (72)
- 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease (73)
- Guidelines for the Primary Prevention of Stroke (2010) (74)
- Guidelines for the Management of Aneurysmal Subarach noid Hemorrhage (2012) (76)
- Guidelines for the Early Management of Patients With Acute Ischemic Stroke (2013) (78)
- Guidelines for the Prevention of Stroke in Women (2014) (79)
- Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack (2014) (81)
- 2014 ACC/AHA Guideline on Perioperative Cardiovas cular Evaluation and Management of Patients Undergoing Noncardiac Surgery (86)

Additional Resources

- Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association (2015) (92)
- Guidelines for the Primary Prevention of Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association (2014) (93)

DISCLOSURES

Writing Group Disclosures

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Michael W. Rich	Washington University School of Medicine	NIA*; NHLBI*	None	None	None	None	None	None
Deborah A. Chyun	New York University	None	None	None	None	None	Qatar National Research Fund*	None
Karen P. Alexander	Duke University Medical Center	None	None	None	None	None	None	None
Daniel E. Forman	University of Pittsburgh Medical Center	None	None	None	None	None	None	None
Dalane W. Kitzman	Wake Forest University School of Medicine	NIH†; Novartis†	None	None	None	Gilead, Inc. Stock Ownership†; Relypsa Inc.*	GSK*; Relypsa*; Regeneron*; AbbVie†; DC Devices*; Abbott Pharmaceuticals*; Actavis*; ICON†	None
Mathew S. Maurer	Columbia College of Physicians and Surgeons	None	None	None	None	None	None	None
James B. McClurken	Doylestown Health Heart Institute	Silver AMI*	None	None	None	None	None	None
Barbara M. Resnick	University of Maryland	None	None	None	None	None	None	None
Win K. Shen	Mayo Clinic	None	None	None	None	None	None	None
Adam H. Skolnick	NYU School of Medicine	None	None	None	None	None	None	None
David L. Tirschwell	Harborview Medical Center	St. Jude Medical†; Bayer*	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.
*Modest.
†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Jeffrey L. Anderson	Intermountain Healthcare	None	None	None	None	None	None	None
Susan Bell	Vanderbilt University	NIH/NICHD (2K12HD043483-11)†	Eisenstein Women's Heart Fund*	None	None	None	None	None
James Blankenship	Geisinger Medical Center	None	Tryton Medical*; Abiomed*; AstraZeneca*; Boston Scientific*; Regado Biosciences*; Volcano*; Abbott Vascular* (Principal Investigator at Geisinger Medical Center for multicenter industry-funded research trials sponsored by these companies)	None	None	None	None	None
Joseph P. Drozda	Mercy Health	None	None	None	None	None	None	My nondependent son is a sales representative for Boston Scientific Corporation†

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Continued

Reviewer	Employment	Research Grant	Other Research Support	Speakers Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Andrew E. Epstein	University of Pennsylvania	Biotronik†; Boston Scientific†; Medtronic; Sorin Medical†; St. Jude Medical†	None	None	Yes (1 current case)*	None	Boston Scientific†; Medtronic†; St. Jude Medical†; Population Health Research Institute*	None
Lee A. Fleisher	University of Pennsylvania	None	None	None	None	None	Member, Medical Advisory Board to Technical Expert Panel of Blue Cross/ Blue Shield Association*	None
Rebecca Gary	Emory University	None	None	None	None	None	None	None
Sarah Goodlin	Portland VAMC	Medtronic*	None	None	None	None	None	None
Lawrence Izzo	State University of New York at Buffalo; Erie County Medical Center	None	None	None	None	None	None	None
Mariell Jessup	University of Pennsylvania Heart and Vascular Center	None	None	None	None	None	None	None
Glenn N. Levine	Baylor College of Medicine; Michael E. DeBakey Medical Center	None	None	None	None	None	None	None
Patrick O'Gara	Brigham and Women's Hospital, Boston, MA	NHLBI, Cardiothoracic Surgery Network†	None	None	None	None	None	None
Catherine M. Otto	University of Washington School of Medicine	None	None	None	None	None	None	None
Lawrence Rudski	Jewish General Hospital, Montreal, Quebec	None	None	None	None	None	None	None
Nanette Wenger	Emory University School of Medicine	Gilead Sciences†; NHLBI†; Pfizer*	None	None	None	None	Amgen*; AstraZeneca*; Gilead Sciences†	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.
*Modest.
†Significant.

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