Electrophysiology and heart rhythm disorders in older adults

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1 Introduction

Heart rhythm disorders, including bradyarrhythmias, atrial fibrillation (AF), and ventricular arrhythmias, become increasingly common with aging and represent important causes of morbidity and mortality among older adults. [1–3] Older adults are particularly predisposed to these conditions due to the high prevalence of cardiovascular disease in conjunction with age-related changes that occur in the heart and cardiac conduction system.

Management of heart rhythm disorders often differs in older compared to younger individuals due to reduced life expectancy, multimorbidity, polypharmacy, and increased vulnerability to adverse effects of therapies. The presence of geriatric syndromes, particularly frailty, [4] and cognitive impairment, [5,6] which have been increasingly recognized as important factors associated with poor outcomes in many cardiovascular conditions, further contribute to the complexity of decision-making in this vulnerable population. Accordingly, this review seeks to describe the evaluation and treatment of common rhythm disturbances among older adults.

2 Bradyarrhythmias

2.1 Description

With age, there are important changes in the conduction system that increase susceptibility to bradyarrhythmias, including calcific and fibro-fatty infiltration of the conduction system, reduction in the number of functioning pacemaker cells, impaired intracellular calcium handling, and blunted adrenergic responsiveness. [7] Comorbidities warranting medications that affect the conduction system also contribute to the increased incidence of bradyarrhythmias among older adults. Consequently, up to 70% of patients undergoing pacemaker implantation are aged at least 70 years. [2]

Bradyarrhythmias, which are primarily caused by sinus node dysfunction and/or atrio-ventricular (AV) block, can lead to hemodynamic compromise from decreased cardiac output. Manifestations include dizziness, lightheadedness, and syncope. Bradyarrhythmias can also present as shortness of breath, exercise intolerance, fatigue, or (less commonly) chest pain. In the setting of concomitant AF, bradyarrhythmias may occur as a “tachy brady syndrome”.

In patients with suspected bradyarrhythmias, the history and physical examination with special attention to linking symptomatology to the bradyarrhythmia are critical, as indications for therapy are often predicated on the presence of associated symptoms. As with any suspected arrhythmia, the ECG is the diagnostic study of first choice. Patients with severe symptoms, such as syncope, may require hospitalization with cardiac telemetry. For ambulatory patients, Holter monitors and event monitors may be useful for detecting bradyarrhythmias. An implantable loop recorder (ILR), which can provide monitoring for up to three years, may also be considered when short-term monitoring has not revealed a cause of recurrent symptoms. [8] Assessing for chronotropic incompetence by performing a formal exercise stress test can also be beneficial, as early stages of sinus node dysfunction may manifest only during exercise.

2.2 Management

The first step in the management of bradyarrhythmias is removal of any inciting cause if present. Causes of bradyarrhythmias are shown in Table 1. Bradyarrhythmias may be precipitated or exacerbated by β-blockers or non-dihydro-
Table 1. Causes of bradycardia in older adults.

| Intrinsic causes                  | Extrinsic causes |
|----------------------------------|------------------|
| Sick sinus syndrome              | Drugs            |
| Conduction system disease        | Autonomic influences |
| Coronary artery disease          | Electrolyte disturbances |
| Cardiomyopathy                   | Hypothyroidism    |
| Infiltrative disorders           | Stroke           |
| Collagen vascular disease        | Increased intracranial pressure |
| Inflammatory processes           | Hypothermia       |
| Surgical trauma                  | Sepsis           |
| Athletic heart                   |                  |

pyridine calcium channel blockers, which are frequently prescribed to older adults for treatment of hypertension, coronary artery disease, atrial fibrillation, or heart failure. Other medications associated with bradycardia include digoxin, clonidine, most antiarrhythmic drugs (AADs) especially amiodarone, and acetylcholinesterase inhibitors. Hypothyroidism and hypothermia are other potentially reversible causes of bradycardia.

When a reversible cause of symptomatic bradycardia cannot be identified, pacemaker implantation is often appropriate. For sinus node dysfunction, pacemaker implantation carries a class I indication when there is documented symptomatic bradycardia or symptomatic chronotropic incompetence, and a class II indication when the heart rate is < 40 beats/min while awake. For AV-block, pacemaker implantation carries a class I indication in the setting of 3rd degree or advanced 2nd degree block with symptomatic bradycardia or associated ventricular arrhythmias, an escape rhythm originating below the AV-node or with a rate < 40 beats/min or with pauses ≥ 3 s (≥ 5 s in AF), an associated neuromuscular disease, or following cardiac surgery without expectation for resolution.

Pacemaker implantation ensures a sufficient ventricular rate to maintain adequate cardiac output, thereby preventing adverse events related to bradycardia (e.g., falls, syncope), increasing exercise capacity, and enhancing quality of life. Although the addition of an atrial lead and/or second ventricular lead is not required to maintain cardiac output, it may improve long-term outcomes. In sinus node dysfunction, the addition of an atrial lead maintains AV-synchrony, reduces the incidence of atrial fibrillation, and decreases hospitalization rate. In AV-block, the addition of a second ventricular lead to pace the left ventricle and minimize ventricular dyssynchrony has been shown to benefit select patients, including those with symptomatic systolic heart failure (left ventricular ejection fraction ≤ 35%) and prolonged QRS on guideline-directed medical therapy, and those with mild systolic dysfunction with anticipated high frequency of pacing. Albeit limited, available evidence indicates that older adults derive comparable benefit from cardiac resynchronization therapy as younger adults. Dual chamber pacemakers and resynchronization therapy should therefore be considered in eligible patients, weighing the benefit against the potential for a slightly increased risk of peri-procedural complications and shorter battery life associated with placement of additional leads.

For patients who do not require an additional lead, a leadless pacemaker, which requires a less invasive procedure for implantation, may be a viable option. With recent Food and Drug Administration approval of the first leadless pacemaker in the USA, and ongoing studies assessing its safety and efficacy in predominantly older patients, leadless pacemakers may soon play an increasing role in managing older adults with indications for pacemakers.

3 Atrial fibrillation

3.1 Description

The prevalence of AF increases with age, most commonly occurring in older adults aged at least 65 years, with up to half occurring among those 75 years or older. This relates in part to age-related changes in atrial tissues mediated by chronic inflammation and other factors leading to fibrosis and associated conduction abnormalities that provide substrate for the electrical disarray that characterizes AF. Hypertension and structural heart disease, both of which increase with age, can lead to additional maladaptive changes in the atria, further predisposing to the development of AF.

Symptoms associated with AF range from none to severe and life-threatening. Common symptoms include palpitations, lightheadedness, chest discomfort, shortness of breath, fatigue, or impaired activity tolerance. Less commonly, syncope, heart failure, or stroke may be the presenting manifestation of AF. The abrupt onset of AF can cause syncope or heart failure due to reduced stroke volume and cardiac output. AF is also a potent risk factor for embolic stroke as a result of stasis of blood and thrombus formation in the left atrial appendage. Consequently, AF is associated with adverse outcomes, even after controlling for age and comorbidities.

Diagnostic studies should include an ECG and an echocardiogram to evaluate chamber sizes, left and right ventricular systolic and diastolic function, valve function, and pulmonary artery pressure. Routine laboratory studies should include a complete blood count, comprehensive metabolic profile, and thyroid-stimulating hormone assay. Additional
studies such as a stress test, cardiac catheterization, or sleep study may be warranted in selected cases.

### 3.2 Stroke prevention

The management of AF centers around two major issues—stroke prevention and control of symptoms. Risk factors for stroke in patients with AF have been well-characterized. Contemporary risk stratification tools include the CHADS2,[22] and the CHA2DS2-VASc scores,[23] which account for select comorbidities as well as age (Table 2). The CHA2DS2-VASc score highlights the importance of age by denoting increased risk for age $\geq 65$ years,[24,25] and by assigning extra weight (2 points) to age $\geq 75$ years.[26] Importantly, all women aged $\geq 65$ years and all men aged $\geq 75$ years have CHA2DS2-VASc scores of $\geq 2$ and are therefore appropriate candidates for anticoagulation unless contraindicated.

While age is associated with increased risk of stroke, it is also associated with an increased risk of bleeding. Thus, all commonly used bleeding risk stratification tools, including HEMORRH2GAGES,[27] HAS-BLED,[28] and ATRIA,[29] incorporate age into their models. These models also include prior bleeding, comorbidity, and history of alcohol use, underscoring the importance of factors beyond age alone. Coronary artery disease, which is present in about 30% of patients with AF,[30] may also have implications for bleeding risk, as the use of anti-platelet agents (e.g., aspirin, thienopyridines) increases the risk of bleeding when combined with anticoagulation.[31] The risk for falls should also be considered when initiating anticoagulation, although a study of Medicare beneficiaries demonstrated that the benefits of anticoagulation usually outweigh the risks even among those at high fall risk.[32] Since there is an inherent tension between the benefits and risks of anticoagulation, a frank discussion of these issues should occur prior to initiating anticoagulation therapy. Ongoing discussion regarding continuation of anticoagulation as overall prognosis changes is also warranted, with discontinuation of anticoagulation a being reasonable option when patients approach end-of-life.

Novel oral anticoagulants (NOACs) offer alternatives to warfarin without the need for routine monitoring of the international normalized ratio (INR). Among those aged 75 years and older, NOACs demonstrated similar (dabigatran 110 mg, rivaroxaban, edoxaban 30 mg) or better (dabigatran 150 mg, apixaban, edoxaban 60 mg) stroke prevention efficacy, with similar (dabigatran 150 mg, edoxaban 30 mg) or less bleeding (dabigatran 110 mg, rivaroxaban, apixaban) compared to warfarin.[33–36] When prescribing NOACs to older adults, it is important to choose the appropriate dose, as many older adults will require adjustment based on age, body weight, and/or renal function. Although the lack of reversal agents for the factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) is a potential limitation of their use in older patients, such agents are under development and likely to become available in the next few years.[37]

For some patients who are not candidates for anticoagulation, percutaneous left atrial appendage closure may represent a viable alternative. As most strokes in AF originate from thrombus in the left atrial appendage, closing or excluding the appendage from the circulation has the potential to prevent embolic strokes. Accordingly, several such devices have been developed,[38] and the WATCHMAN device has been approved for use in the United States.[39] While these devices appear to be effective in preventing stroke among a predominantly older population, the risk for procedural complications and the ongoing need for anti-platelet therapy must be considered prior to pursuing such a procedure. Whether improvements in technology and procedural expertise will ultimately make percutaneous left atrial appendage closure the method of choice for stroke prevention among older adults with contraindications to anticoagulation remains to be seen.

#### 3.3 Rate and rhythm control

From a clinical perspective, AF may be managed by a rate or rhythm control strategy. Based on several studies including the landmark AFFIRM trial,[40] a rate control strategy appears safer and as effective as rhythm control (i.e., attempting to maintain sinus rhythm) with respect to clinical outcomes, and is therefore recommended as first-line treatment for AF in asymptomatic or mildly symptomatic patients. Guidelines designate beta-blockers and non-dihydropyridine calcium channel blockers as having a class I indication for achieving rate control.[41] Among older adults, rapid up-titration or high doses of these agents may induce hypotension and falls due to age-related attenuation of the baroreflex response, impaired responsiveness to adrenergic

| Table 2. Components of CHADS2 and CHA2DS2-VASc scores. |
|----------------|----------------|
| CHADS2          | CHA2DS2-VASc   |
| CHF             | 1              |
| Hypertension    | 1              |
| Age $\geq 75$ yrs | 2              |
| Diabetes        | 1              |
| Stroke          | 2              |
| Vascular disease | 1              |
| Age $\geq 65$ yrs | 1              |
| Female sex      | 1              |

CHF: congestive heart failure.
activity, autonomic dysfunction, and conduction system disease. Given this risk, a lenient rate-control strategy of < 110 beats/min is acceptable in the absence of significant symptoms (e.g., palpitations), coronary artery disease, or heart failure based on results of the RACE II trial, which demonstrated lenient control to be at least as safe and effective as a strict rate control strategy of < 80 beats/min.

Although a rhythm control strategy may be associated with higher functional status and quality of life metrics that are particularly important among older adults, AADs are associated with high incidence of adverse events among older adults due to the potential for drug interactions, unpredictable pharmacokinetics and pharmacodynamics, and variable renal function. In an AFFIRM subgroup analysis of patients older than 70 years, all-cause mortality was higher in the rhythm control group compared to the rate-control group, hypothesized to directly relate to the use of AADs in the rhythm-control arm. AADs that require particular caution among older adults include IC agents (i.e., flecainide and propafenone), as they are contraindicated in the presence of structural heart disease and dronedarone, which has been associated with an increased risk of cardiovascular events among older adults with pre-existing cardiovascular disease. Importantly, the use of a rhythm-control strategy does not obviate the need for anticoagulation. Thus, although the American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines for the management of AF state that AAD therapy may be selected to reduce the frequency and duration of AF and improve quality of life, the potential for adverse events from AADs is an important consideration in older adults.

Other approaches to rhythm control may include electrical cardioversion (independent of or in conjunction with AADs), catheter ablation, or surgical ablation. Electrical cardioversion requires the administration of anesthetic agents, which have attendant risks, and may be associated with stroke unless effective anticoagulation is maintained prior to and following the procedure. Although catheter ablation is recommended for patients with symptomatic AF refractory or intolerant to AADs when rhythm control is desired, data are limited on its safety and efficacy in older adults who commonly have large atria and fibrosis that may reduce likelihood of restoring and maintaining sinus rhythm. The Cox-maze procedure, which is comprised of making several incisions in the atria to isolate and exclude myocardial tissue thereby preventing AF propagation, offers yet another strategy, but is usually reserved for patients undergoing cardiac surgery for other indications. Therefore, the use of rhythm control, even without AADs, may not be optimal for older adults in the absence of persistently symptomatic AF despite efforts to achieve effective rate control.

4 Ventricular arrhythmias

4.1 Description

The prevalence of premature ventricular depolarizations (PVD) increases with age, in part due to the age-related increase in structural heart disease. In the absence of bothersome symptoms or very high PVD burden, no specific treatment is required. Potentially life-threatening ventricular arrhythmias, including ventricular tachycardia (VT) and ventricular fibrillation (VF), almost always occur in the setting of structural heart disease, such as ischemic or hypertensive cardiomyopathy.

Symptoms and diagnostic evaluation of ventricular arrhythmias are generally similar in older and younger patients. As with bradyarrhythmias, Holter monitors, event monitors, and ILRs are useful for confirming the association of symptoms with arrhythmias. Invasive electrophysiological testing is rarely necessary but may be useful in patients with unexplained syncope if a ventricular arrhythmia is suspected.

4.2 Implantable cardioverter-defibrillator

In appropriately selected patients, implantable cardioverter-defibrillators (ICDs) reduce mortality for both primary and secondary prevention of sudden cardiac death (SCD). For primary prevention, ICDs are recommended for patients with New York Heart Association class II-III heart failure, left ventricular ejection fraction ≤ 35% with at least three months of guideline-directed medical therapy and/or at least 40 days following a myocardial infarction, and life expectancy of at least 12 months with reasonable functional status (Table 3). For secondary prevention, ICDs are recommended for survivors of cardiac arrest from VT or VF following an evaluation to exclude reversible causes, those with sustained symptomatic VT, and those with unexplained syncope where the likelihood of VT or VF is high.

Although the guidelines do not distinguish indications for ICD therapy based on age, very few patients aged ≥ 75 years were enrolled in the ICD clinical trials. As a result, the evidence base for ICDs in elderly patients is much less robust than in younger individuals, and the benefit of ICDs declines with age due to competing risks for death (e.g., pneumonia, hip fracture) and the reduced proportion of SCD events that are caused by a ventricular arrhythmia (vs. asystole or pulseless electrical activity) in older adults. These observations highlight the importance of patient selection. As noted
Table 3. ICD for primary prevention of sudden cardiac death.

| Class I indications                                                                 | Contraindications (Class III Indications)                                                                 |
|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| LVEF ≤ 35% due to ischemic or nonischemic cardiomyopathy, at least 40 days post-MI and in NYHA class II or III | Anticipated survival with reasonable functional status < 1 year                                          |
| LVEF < 30% due to prior MI, at least 40 days post-MI, and NYHA class I                | Significant psychiatric illness that may be aggravated by an ICD                                          |
| LVEF < 40% due to prior MI with nonsustained VT and inducible sustained VT or VF on electrophysiology study | Drug refractory NYHA class IV heart failure in patient who is not a candidate for transplantation or CRT-D|
|                                                                                     | Syncope of undetermined cause in the absence of structural heart disease or inducible ventricular arrhythmia |

CRT-D: cardiac resynchronization therapy + defibrillator device; ICD: implantable cardioverter-defibrillator; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; VF: ventricular fibrillation; VT: ventricular tachycardia.

above, an ICD is not indicated if the life expectancy with acceptable functional status is less than one year.[9] On the other hand, age alone should not drive the decision to implant an ICD, as survival after ICD insertion may be substantial even among octogenarians.[55] It is therefore essential to engage in shared decision-making regarding ICD implantation. Beyond age and clinical factors, patient values and preferences must be considered, as the desire for longer life may not outweigh the preference for a painless death (as typically experienced with SCD), especially in the setting of declining health and functional status.[56] Importantly, these discussions should occur not only at initial implantation, but also when there is a need for generator replacement, as overall prognosis and patient preferences may change over time.

4.3 End-of-life care

Since ICDs have the potential to prolong life, ICD management should be addressed in advance care planning and end-of-life discussions.[57] As prognosis declines, ICD deactivation may be considered to prevent distress to patients and their families. While discussions about ICD deactivation promote patient autonomy,[57] few patients report engaging in a dialogue with their physicians regarding deactivation even as death becomes imminent.[58] Consequently, terminally-ill patients with ICDs often experience unwanted shocks.[59] Thus, there is a need to better incorporate device deactivation into advance directives and end-of-life discussions.

5 Summary

The prevalence of heart rhythm disorders, including supraventricular and ventricular arrhythmias, as well as bradyarrhythmias, increases with age, in part due to age-related changes in the heart and conduction system, and in part due to comorbidities common to older adults. Although clinical features and treatment options for heart rhythm disorders are generally similar in older and younger patients, older adults are more likely to have multiple coexisting conditions and geriatric syndromes that may impact the benefit-to-risk ratio for both diagnostic and therapeutic interventions. In addition, older adults tend to have shorter life expectancy and may place greater emphasis on maintaining quality of life than on maximizing length of life. For these reasons, it is essential that each patient's preferences and goals of care be elicited and integrated into the management plan utilizing a process of shared decision-making.

6 Clinical pearls

The management of heart rhythm disorders often differs in older compared to younger adults due to reduced life expectancy, multimorbidity, polypharmacy, and increased vulnerability to adverse effects of therapies.

The presence of geriatric syndromes, especially frailty and cognitive impairment, contribute to the complexity of decision-making in this vulnerable population.

For bradyarrhythmias, a pacemaker may be indicated for sinus node dysfunction or AV-block to prevent falls and improve quality of life; additional lead placement or opting for a leadless pacemaker may be beneficial in select patients.

The decision to initiate (and continue) anticoagulation for AF must incorporate the risks for stroke and bleeding, as both increase with advanced age and in the presence of comorbidities common to older adults.

Although NOACs may offer increased convenience, efficacy, and safety compared to warfarin, attention must be paid to choosing the appropriate dose, as many older adults will require adjustment based on age, body weight, and/or renal function.

In older adults, a lenient rate-control strategy may be better tolerated than strict rate control or rhythm-control strategies unless there are compelling indications for the latter.

Because the benefit of ICD therapy declines with age, patient values and preferences must be considered in conjunction with the clinical scenario prior to implantation.
Since ICDs have the potential to prolong life, ICD management should be addressed in advance care planning and end-of-life discussions.

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