

Rhythm-control vs rate-control in the elderly: When to do it and which drug to prefer?

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Abstract

Atrial fibrillation (AF) is a relevant cardiovascular condition that is more prevalent in the elderly patients aged over 65 years. AF, with abnormal rate and rhythm can cause symptoms directly or indirectly by exacerbating other frequently coexisting cardiac conditions such as valvular heart disease, hypertension, ischemic cardiomyopathy, dilated cardiomyopathy, and hypertrophic cardiomyopathy. Evidence suggests that aging-related cardiovascular changes predispose the elderly to AF. Current therapeutic options such as antiarrhythmic drugs have not been extensively evaluated in the elderly population. Emerging pharmacological and non-pharmacological treatment options for the management of AF, such as dronedarone or catheter ablation, are of particular interest in the elderly. The present paper reviews the pathophysiology, diagnosis, and the management of AF in the elderly patient.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice and its prevalence increases with age, making it particularly frequent in patients older than 65 years. For patients older than 80 years, the corresponding rate is approximately 10% [1]. Furthermore, 70% of individuals with AF are between the age of 65 and 85 years. AF is a major risk factor for serious cardiovascular events such as stroke and heart failure, and even if it cannot be considered directly life threatening, it is undoubtedly related to an increased risk of death. In the Framingham study, the total mortality odds ratio was 1.5 for male and 1.9 for female patients with AF, even after adjustment for age and other risk factors [2]. In addition, the morbidity of the elderly patients suffering from AF is of considerable importance, because these patients exhibit increased and, often, long hospitalizations due to stroke, heart failure, adverse effects related to antiarrhythmic therapy, and need for pacemaker implantations. Even though this arrhythmia has been acknowledged

since long ago, its treatment and management remain a challenge even in the modern era. Recent breakthroughs in drug therapy and invasive techniques have opened new perspective in the setting of AF. Elderly patients, who were often excluded from trials are now actively participating in various studies, thus giving medical science new solutions concerning the management and treatment of this group of age.

Pathophysiology and diagnosis of atrial fibrillation

The exact explanation for increased prevalence of AF is unknown. Aging heart, characterized by myocardial fibrosis and atrial dilation, is a proper field for AF, and conditions that predispose to AF (such as hypertension, heart failure and ischemic heart disease) are more prevalent in the elderly. The arrhythmia creates electrical and structural remodeling at the atrial level by shortening effective refractory period, depressing the intra-atrial conduction, and depriving its contractile function [3]. Structural heart disease enforces atrial chamber abnormality, and this explains the higher prevalence of AF in patients with underlying cardiovascular conditions such as valvular heart disease, hypertension, ischemic cardiomyopathy, dilated cardiomyopathy, and hypertrophic cardiomyopathy [4]. Obstructive sleep apnea and obesity are also independent risk factors for AF [5,6]. The electrical and structural remodeling determines the perpetuation of AF and the progression from paroxysmal to persistent and permanent forms. The longer one waits to initiate a rhythm treatment strategy, the more difficult it is to regain sinus rhythm.

A single 12-lead electrocardiogram (ECG) is mandatory to set the diagnosis of AF. Because the elderly patients are often asymptomatic, AF is frequently a random finding [7]. If AF is suspected, repeated ECGs, ambulatory monitoring, or other long-term monitoring strategies are advised. In the case of first-diagnosed AF, diagnostic evaluation should further continue with chest X-ray, transthoracic, or transesophageal echocardiography and blood tests, including thyroid hormones.

Rate-control in atrial fibrillation

In the elderly patients, especially the asymptomatic ones, rate control is the first-line therapy [8]. As shown in the AFFIRM substudy, β -blockers are the most effective at achieving that goal [9]. Nondihydropyridine calcium channel blockers (diltiazem or verapamil) can be administered as an alternative. Digoxin is recommended in acute heart failure [8], but has been proven to be an independent risk factor for death in patients without heart failure and should be used cautiously in the elderly in whom renal function is often compromised. Amiodarone can also be used for rate control, but has considerable side effects, most of them extracardiac [8]. A stricter rate control does not seem to improve morbidity and mortality [10,] and so proper use of these drugs is recommended in order to avoid excess bradycardia or atrioventricular block.

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Rhythm-control in atrial fibrillation

In an elderly patient with recurrences of AF despite receiving rhythm control medication, further attempts at restoring sinus rhythm are not suggested. Cardioversion, whether electrical or pharmacological, is related to serious side effects in the elderly and unless AF shorter than 48 hours in duration, OAC must be administered for at least 3-4 weeks. Pharmaceutical cardioversion requires medication that has serious side effects and contraindications. Amiodarone is the safest choice in pharmaceutical cardioversion in the elderly. As featured in major studies, no significant difference in survival was found using rhythm or rate control in patients older than 65 years with at least one stroke risk factor [8,9,11]. While there is a wide range of antiarrhythmic drugs used to maintain sinus rhythm, in the elderly, there are limitations because of their coexisting heart, renal, or hepatic diseases. Antiarrhythmic agents have been associated with serious adverse side effects, particularly the induction of proarrhythmia. Proarrhythmia, caused by class I and III agents, is manifested as a rise in ventricular ectopy, QT interval prolongation, torsades de pointes, monomorphic ventricular tachycardia, or excess bradycardia. Studies have shown that quinidine, flecainide, sotalol, and dofetilide are the antiarrhythmics most prone to ventricular proarrhythmia [12]. Class I antiarrhythmic drugs are generally not recommended in the elderly. As observed in the CAST study [13], flecainide, among other Ic drugs, increased mortality in comparison to placebo, in patients who suffered from myocardial infarction. Therefore, flecainide and propafenone must be given exclusively to patients without structural heart disease. Administration of these drugs to the elderly must be performed cautiously, given the high probability of underlying coronary artery disease. When administered in outpatients, QRS duration must be monitored closely: QRS widening must not exceed 150% of the baseline QRS [14]. Exercise testing should be performed 1 or 2 weeks after initiation, as it may disclose myocardial ischemia, QRS widening at high rates, exercise-induced proarrhythmia [8,14,15]. In the case of coronary artery disease without heart failure, sotalol, dofetilide, amiodarone, and dronedarone (class III antiarrhythmic agents) can be used for maintaining sinus rhythm [8,14,15]. Dronedarone should be given cautiously to elderly patients [16]. The PALLAS study has shown that dronedarone has been related to an increased risk of cardiovascular events in the following groups of patients: i) 65 years or older with permanent AF and either coronary artery disease, previous stroke, or heart failure and ii) 75 years or older with hypertension and diabetes [16]. Patients with AF and heart failure or left ventricular dysfunction are limited to amiodarone and dofetilide. Those with substantial left ventricular hypertrophy (left ventricular wall thickness >13 mm) can only receive amiodarone [8]. When class III agents are administered, QTc interval must be monitored and must remain below 520 ms. In any case of antiarrhythmic drug use, follow-up must include measurement of serum creatinine, and potassium regularly. Renal impairment can increase proarrhythmia and also requires dosage adjustment of dofetilide and sotalol [8,14,15].

Catheter ablation of atrial fibrillation in the elderly

Left atrial catheter ablation has lately proven to be a considerable therapeutic option in maintaining sinus rhythm in patients suffering from AF [17]. However, AF catheter ablation has not been yet commonly established in the elderly population [8]. Due to concerns about efficacy and safety of this method, patients aged 75 years and over were

previously excluded from many catheter ablation trials. So far, the main volume of data concerning the safety and efficacy of left atrial ablation has been derived from studies and trials focused on younger patients without heart disease or comorbidities [18]. Catheter ablation is strongly contraindicated in patients with thrombus in the left atrium or in patients who cannot receive anticoagulation for at least 6-8 weeks after the procedure. In a large worldwide survey, major complications of catheter ablation, including death, cardiac tamponade, strokes, and transient ischemic attacks were reported in 4.5% of cases [19]. Then again, rate control strategy in the elderly may induce extreme bradycardia, while antiarrhythmic drugs used to achieve rhythm control are prone to proarrhythmia and drug interactions. Evolution in AF ablation techniques and improved efficacy have given the elderly patients an alternative treatment for AF. Recent studies have demonstrated similar rates of success and adverse events using radiofrequency catheter ablation between the elderly and younger patients [20-22]. There are some obvious disadvantages of this method. Some patients may relapse and so a second procedure will be required in order to maintain normal sinus rhythm [22]. Also, the need for anticoagulation and detection of asymptomatic AF episodes [22] will have to be further evaluated. Cryoballoon ablation also seems to be a technique getting clinical space. The main advantage over radiofrequency ablation is the lower risk of pulmonary stenosis or esophageal injury. The most common complication of the latter technique is phrenic nerve palsy [23]. Atrioventricular node (AVN) ablation and pacemaker implantation is a last resort treatment in the elderly patients, especially the highly symptomatic ones. As shown in the PABA-CHF study, left atrial catheter ablation was superior to AVN ablation with biventricular pacing in patients with heart failure who had drug-refractory AF [24]. In another study the authors compared the long-term results of elderly patients with medically refractory paroxysmal AF to either AVN ablation plus single-chamber pacemaker or catheter ablation of AF [25]. AF was better controlled in the group with AVN ablation and pacemaker implantation than in the group with AF ablation [25]. However, AVN ablation and pacemaker implantation was associated with a higher incidence of persistent AF and heart failure than catheter ablation of AF in the very long-term follow-up.

Conclusions

Over the past decades, novel medications and therapies have been administered to the elderly patients with AF. This subgroup of patients who were neglected and undertreated now occupy the center stage. Therapies must be tailored to elderly patients, with particular attention to structural heart disease and renal failure. The decision between rate or rhythm control in the elderly is particularly difficult because lack of demonstration of clear superiority of each strategy, in this specific population.

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