Treatment of Ventricular Arrhythmias and Use of Implantable Cardioverter-Defibrillators to Improve Survival in Older Adult Patients with Cardiac Disease

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KEYWORDS

• Ventricular arrhythmia • ICD • Ablation • Antiarrhythmic drugs • Autonomic modulation

KEY POINTS

- Ventricular arrhythmias in patients with cardiac disease are caused by similar mechanisms regardless of the underlying disease and are treated much the same way regardless of age.
- Antiarrhythmic drugs and catheter ablation are accepted therapies to prevent recurrence but do not prevent sudden cardiac death.
- The implantable cardioverter-defibrillator is the only therapy proved to prevent mortality in patients with ventricular arrhythmias and cardiac disease; however, it is unclear whether this benefit is as robust in the elderly.

INTRODUCTION

The causes and substrates for heart failure (HF) are myriad and are discussed elsewhere in this issue of *Heart Failure Clinics*. The risk of ventricular arrhythmia (VA) depends on the cause and severity of HF and the degree of ventricular dysfunction. Structural heart disease (SHD) can take many forms. Ischemic cardiomyopathy (ICM) occurs in the setting of healed myocardial infarction (MI), leaving behind an area of fibrotic scar. This condition is in contrast with nonischemic cardiomyopathy (NICM), a term that encompasses many different causes, such as viral cardiomyopathy (CMP), cardiac sarcoidosis, and idiopathic dilated cardiomyopathy. Frequently, the exact cause of NICM goes undetermined. Therefore, this group is treated as a whole.

SUBSTRATE AND MECHANISM OF VENTRICULAR ARRHYTHMIAS

The initiation and maintenance of VA in SHD is a complex process that requires an abnormal electrical milieu (substrate), an initiating event (such as ectopic beats), and the modulating factors that influence both (such as autonomic balance). Much is known about the substrate and its role in

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arrhythmogenesis. A common end point of many CMPs is the development of ventricular fibrosis and scar. Be it scar from MI, fibrosis from infiltrative CMP such as cardiac sarcoidosis, or fibrofatty replacement in arrhythmogenic right ventricular cardiomyopathy, this process is the common substrate for VA of all causes. Fibrotic pattern varies depending on the cause of SHD. Although MI causes a predominantly subendocardial scar in a vascular distribution, NICM-associated fibrosis can be midmyocardial or epicardial without a correlation to coronary artery territory.[1] Scar deposition is rarely a homogeneous process; usually, surviving myocardial fibers are interspersed in areas of fibrosis.[2] Although these surviving fibers do not participate in systolic function, they are capable of impulse conduction and do so during sinus rhythm.[2–4]

The best-studied process for ventricular tachycardia (VT) is that of monomorphic VT (unchanging QRS morphology and rate) in chronic healed MI. Conduction in infarcted areas is generally slow because of decreased gap junctions at the intercalated disks and also because of more frequent conduction between parallel myocytes, leading to nonlinear, zigzag conduction.[5,6] These areas of surviving myocardium within scar display longer refractory periods and thus encounter transient unidirectional block caused by premature ventricular contractions (PVCs) or changes in heart rate (such as supraventricular tachycardia).[7]

The most important modulating factor behind VA is the sympathetic nervous system. The exact mechanism by which catecholamines influence VA in SHD is not clearly delineated in humans. In addition to enhancement of ectopic activity (caused by both enhanced automaticity and triggered activity) that may initiate sustained VA,[8–10] inhomogeneities in sympathetic innervation of infarcted areas can lead to ectopy as well as changes in potassium channel activity[11] and thus a dispersion of refractory periods.

MEDICAL THERAPY

Antiarrhythmic Drugs

When discussing management of VA in HF, the greatest focus is on sustained arrhythmia and the prevention of sudden cardiac death (SCD). Because no AAD has been reliably shown to prevent SCD, an ICD is indicated in most patients with sustained VA and HF.[12] Several trials have investigated AAD for treatment of complex ventricular ectopy in patients with SHD (mostly post-MI) before the wide adoption of the ICD. Other randomized trials have focused mostly on comparing AAD selection strategies to reduce mortality in patients who have had a sustained VA, rather than strictly preventing VA recurrence. Additional management considerations pertain to preventing recurrent symptomatic VA episodes, especially those that lead to ICD shocks, which have been associated with increased morbidity and mortality.[13] In the ICD era, AAD use in patients with HF has been relegated to prevention of shocks. Because of the increased SCD risk of the class Ic AAD,[14] these agents (flecainide and propafenone) are largely avoided, even in patients with an ICD.

Ventricular ectopy and nonsustained ventricular tachycardia

Based on the observation that frequent ventricular premature beats (VPBs) in post-MI patients are a marker for mortality,[15–18] several trials were undertaken to determine whether treatment with AAD would be protective in this population. The Cardiac Arrhythmia Suppression Trial (CAST) investigated the effects of the class Ic agents flecainide or encainide versus placebo in patients with prior MI, decreased ejection fraction (EF), and at least 6 VPB/h (average) on Holter monitoring at least 6 days after MI.[14] The primary end point of death or resuscitated cardiac arrest was reached in 63 AAD patients versus 26 on placebo ($P = .0001$). Of these, 43 (AAD) and 16 (placebo) were caused by arrhythmia. Most of the nonarrhythmic end points were caused by MI complicated by cardiogenic shock or HF, suggesting that the negative inotropic effects of these drugs exacerbated the ischemic events.[14] Another class Ic AAD, propafenone, was investigated in the Cardiac Arrest Study Hamburg (CASH) trial, compared with amiodarone, metoprolol, and ICD in patients resuscitated from cardiac arrest caused by sustained VA.[19] The propafenone arm of this trial was terminated early because of a 61% higher all-cause mortality compared with the other arms.[20] Because of these findings, the class Ic AAD are largely avoided in patients with coronary artery disease (CAD) and/or SHD.

Amiodarone is a class III AAD that also has class I, II, and IV effects. The Basel Antiarrhythmic Study of Infarct Survival (BASIS) randomized patients before hospital discharge post-MI who also had asymptomatic Lown class 3 or 4b VAs on 24-hour Holter monitor.[21] Three-hundred and twelve patients were randomized to control, empiric amiodarone, or individualized AAD treatment with several class I and III AAD. Compared with the control group, only amiodarone decreased mortality (5% vs 13%; $P<.05$) and sudden death/sustained VT/ventricular fibrillation (VF) (5% vs 17%; $P<.01$). In the Canadian Amiodarone Myocardial