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Chapter 5

Treatment of Ventricular Arrhythmias

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/57545

1. Introduction

The presence of 3 or more consecutive ventricular premature complexes (VPCs) on an electrocardiogram is ventricular tachycardia (VT) [1, 2]. VT is sustained if it lasts ≥30 seconds and nonsustained if its lasts <30 seconds [2]. Complex ventricular arrhythmias (VA) are VT or paired, multiform, or frequent VPCs. This author diagnoses frequent VPCs if there are an average of ≥30/hour on a 24-hour ambulatory electrocardiogram (AECG) or ≥6/minute on a 1-minute rhythm strip of an electrocardiogram (ECG) [2, 3]. Simple VA are infrequent VPCs and no complex forms.

The prevalence of nonsustained VT diagnosed by 24-hour AECGs varied from 2% to 13% in older persons without cardiovascular disease [1, 4-7], was 9% in 385 older men and 8% in 806 older women with hypertension, valvular disease, or cardiomyopathy [7], and was 16% in 395 older men and 15% in 771 older women with coronary artery disease (CAD) [7]. The prevalence of complex VA in older persons in these studies varied from 16% to 50% in older persons without cardiovascular disease [1, 4-7], was 54% in older men and 55% in older women with hypertension, valvular disease, or cardiomyopathy [7], and was 69% in older men and 68% in older women with CAD [7].

In 104 older persons without cardiovascular disease, complex VA were present on 24-hour AECGs in 33% of persons and on 1-minute rhythm strips in 2% of persons [3]. In 843 older persons, with cardiovascular disease, complex VA were present on 24-hour AECGs in 55% of persons and on 1-minute rhythm strips in 4% of persons [3].

In persons with cardiovascular disease, those with an abnormal left ventricular (LV) ejection fraction [8], with echocardiographic LV hypertrophy [9], or with silent myocardial ischemia [10] have a higher prevalence of VT and of complex VA than those with normal LV ejection fraction, normal LV mass, and no myocardial ischemia.

2. Prognosis of ventricular arrhythmias

In the Baltimore Longitudinal Study of Aging, nonsustained VT or complex VA were not associated with new
coronary events at 10-year follow-up of 98 persons without heart disease [11]. In this study, exercise-induced nonsustained VT was not associated with new coronary events at 2-year follow-up in persons without heart disease [12]. At 5.6-year follow-up in this study, exercise-induced frequent or repetitive VPCs also were not associated with new coronary events in persons without heart disease [13].

Nonsustained VT or complex VA diagnosed by 24-hour AECGs were not associated with new coronary events at 2-year follow-up in 76 persons without heart disease [14] and were not associated with primary ventricular fibrillation (VF) or sudden cardiac death in 86 persons without heart disease [15]. Complex VA diagnosed by 24-hour AECGs or by 12-lead ECGs with 1-minute rhythm strips were also not associated with new coronary events at 39-month follow-up in 104 persons without heart disease [3]. Nonsustained VT or complex VA diagnosed by 24-hour AECGs were not associated with new coronary events at 45-month follow-up of 135 men and at 47-month follow-up of 297 women without cardiovascular disease [7].

Because nonsustained VT or complex VA are not associated with new coronary events in persons without heart disease, asymptomatic nonsustained VT or complex VA in persons without heart disease should not be treated with antiarrhythmic drugs. Because simple VA in persons with heart disease are not associated with new coronary events [3, 7, 11, 14, 15], simple VA in older persons with heart disease should not be treated with antiarrhythmic drugs.

However, patients with VT (sustained or nonsustained) or with complex VA associated with heart disease are at increased risk for developing new coronary events, primary VF, and sudden cardiac death [3, 7, 11, 14-19].

3. Medical therapy

Underlying causes of complex VA should be treated, if possible. Therapy of congestive heart failure (CHF), digitalis toxicity, hypokalemia, hypomagnesemia, hypertension, LV dysfunction, LV hypertrophy, myocardial ischemia by anti-ischemic drugs such as beta blockers or by coronary revascularization, hypoxia, and other conditions may abolish or decrease complex VA. Persons should not smoke or drink alcohol and should avoid drugs that may cause or increase complex VA.

CAD should be treated with aspirin [20-23], with beta blockers [23-28], with angiotensin-converting enzyme (ACE) inhibitors [23, 28-33], and with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) [23, 34-40] unless there are contraindications to these

drugs. The serum low-density lipoprotein (LDL) cholesterol level should be reduced ≥ 50% by high-dose statins (atorvastatin 40to 80 mg daily or rosuvastatin 20 to 40 mg daily) [40].

Age-related physiologic changes may affect absorption, distribution, metabolism, and excretion of cardiovascular drugs [41]. Numerous physiologic changes with aging affect pharmacodynamics with alterations in end-organ responsiveness to cardiovascular drugs [41]. Drug interactions between antiarrhythmic drugs and other cardiovascular drugs are common [41]. There are also important drug-disease interactions [41]. Class I antiarrhythmic drugs have an unacceptable proarrhythmia rate in patients with heart disease and should be avoided. Class III antiarrhythmic drugs should also be used with caution in patients with heart disease since multiple factors may increase proarrhythmia. Except for beta blockers, all antiarrhythmic drugs may cause torsades de pointes (VT with polymorphous appearance associated with prolonged QT interval).

Class I antiarrhythmic drugs are sodium channel blockers. Class Ia antiarrhythmic drugs have intermediate channel kinetics and prolong repolarization. These drugs include quinidine, procainamide, and disopyramide. Class Ib antiarrhythmic drugs have rapid channel kinetics and slightly shorten repolarization. These drugs include lidocaine, mexilitine, tocainide, and phenytoin. Class Ic drugs have slow channel kinetics and have little effect on repolarization. These drugs include encainide, flecainide, moricizine, propafenone, and lorcainide. None of the Class I antiarrhythmic drugs have been found in controlled, clinical trials to reduce sudden cardiac death, total cardiac death, or total mortality.

The International Mexilitine and Placebo Antiarrhythmic Coronary Trial (IMPACT) was a prospective, double-blind, randomized study in survivors of myocardial infarction (MI) in whom 317 persons were randomized to mexilitine and 313 persons to placebo [42]. At 1-year follow-up, mortality was 7.6% for mexilitine-treated patients versus 4.8% for placebo-treated patients [42].

The Cardiac Arrhythmia Suppression Trial (CAST) I was a prospective, double-blind, randomized study in survivors of MI with asymptomatic or mildly symptomatic VA in which 730 patients were randomized to encainide or flecainide and 725 patients to placebo [43]. Adequate suppression of VA by encainide or flecainide was needed before randomization. Despite adequate suppression of VA, at 10-month follow-up, encainide and flecainide significantly increased mortality from arrhythmia or cardiac arrest 3.6 times and significantly increased total mortality 2.5 times[43). Older age increased the likelihood of adverse events, including death, in patients treated with encainide and flecainide[44].

CAST II was a prospective, double-blind, randomized study in survivors of MI with asymptomatic or mildly symptomatic VA in which 581 patients were randomized to moricizine and 574 patients to placebo. [45]. Adequate suppression of VA by moricizine was required before randomization. At 18-month follow-up, the mortality from arrhythmia or cardiac arrest was 8.4% for patients treated with moricizine and 7.3% for patients treated with placebo [45]. The 2-year survival rate was 81.7% for patients treated with moricizine and 85.6% for patients treated with placebo [45]. Older age increased the likelihood of adverse events, including death, in patients receiving moricizine [44].

Aronow et al [46] performed a prospective study in 406 persons with heart disease (58% with prior MI) and asymptomatic complex VA diagnosed by 24-hour AECGs. The prevalence of nonsustained VT was 20%. The prevalence of an abnormal ejection fraction was 32%. The incidence of adverse effects causing cessation of drug was 48% for quinidine and 55% for procainamide. At 24-month follow-up, the incidences of sudden cardiac death, total cardiac death, and of total death were not significantly different in persons treated with quinidine or procainamide or with no antiarrhythmic drug [46]. The incidence of total mortality was 65% for persons treated with quinidine or procainamide and 63% for persons treated with no antiarrhythmic drug. Quinidine or procainamide did not decrease sudden cardiac death, total cardiac death, or total death in comparison with no antiarrhythmic drug in older patients with ischemic or nonischemic heart disease, abnormal or normal LV ejection fraction, and presence versus absence of VT [46].

Moosvi et al [47] performed a retrospective analysis of the effect of empiric antiarrhythmic therapy in 209 resuscitated out-of-hospital cardiac arrest patients with CAD. Of the 209 patients, 48 received quinidine, 45 received procainamide, and 116 received no antiarrhythmic drug. The 2-year sudden death survival was 69% for quinidine-treated patients, 69% for procainamide-treated patients, and 89% for patients treated with no antiarrhythmic drug [47]. The 2-year total survival was 61% for quinidine-treated patients, 57% for procainamide-treated patients, and 71% for patients treated with no antiarrhythmic drug [47].

Hallstrom et al [48] performed a retrospective analysis of the effect of antiarrhythmic drug use in 941 patients resuscitated from prehospital cardiac arrest attributable to VF between 1970 and 1985. Quinidine was given to 19% of patients, procainamide to 18% of patients, beta blockers to 28% of patients, and no antiarrhythmic drug to 39% of patients. There was a 17% increased incidence of death or recurrent cardiac arrest in patients treated with quinidine or procainamide versus no antiarrhythmic drug. Survival was 57% worse for patients treated with procainamide than for patients treated with quinidine [48].

A meta-analysis of 6 double-blind studies of 808 patients with chronic atrial fibrillation who underwent direct-current cardioversion to sinus rhythm showed that the mortality at one year was higher in patients treated with quinidine (2.9%) than in patients treated with placebo (0.8%) [49]. Of 1, 330 patients in the Stroke Prevention in Atrial Fibrillation Study, 127 were receiving quinidine, 57 procainamide, 15 disopyramide, 34 flecainide, 20 encainide, and 7 amiodarone [50]. The adjusted relative risk of cardiac mortality was 1.8 times higher and the adjusted relative risk of arrhythmic death was 2.1 times higher in patients receiving antiarrhythmic drugs [50]. In patients with a history of CHF, the adjusted relative risk of cardiac death was 3.3 times higher and the adjusted relative risk of arrhythmic death was 5.8 times higher in patients receiving antiarrhythmic drugs[50].

Morganroth and Goin [51] performed a meta-analysis of 4 randomized, double-blind controlled trials lasting 2 to 12 weeks in which quinidine (n=502) was compared with flecainide (n=141), mexiletine (n=246), tocainide (n=67), and propafenone (n=53) in the treatment of complex VA. There was an increased risk of mortality in patients treated with quinidine compared with patients treated with the other antiarrhythmic drugs (absolute risk increase = 1.6%) [51].

Teo et al [52] analyzed 59 randomized controlled trials of 23, 229 patients that investigated use of Class I antiarrhythmic drugs after MI. The Class I drugs investigated included quinidine, procainamide, disopyramide, imipramine, moricizine, lidocaine, tocainide, phenytoin, mexiletine, aprindine, encainide, and flecainide. Mortality was 14% higher in patients receiving Class I antiarrhythmic drugs than in patients receiving no antiarrhythmic drugs. None of the 59 studies demonstrated that use of a Class I antiarrhythmic drug decreased mortality in postinfarction patients [52].On the basis of these data, no Class I antiarrhythmic drugs should be used for the treatment of VT or complex VA.

Calcium channel blockers are not useful in treatment of complex VA. Although verapamil can terminate a left septal fascicular VT, hemodynamic collapse can occur if intravenous verapamil is given to patients with the more common forms of reentry VT. Teo et al [52] analyzed randomized controlled trials of 20, 342 patients that investigated the use of calcium channel blockers after MI. Mortality was insignificantly 4% higher in patients receiving calcium channel blockers than in patients receiving no antiarrhythmic drugs [52]. On the basis of these data, no calcium channel blockers should be used in the treatment of VT or complex VA.

Teo et al [52] analyzed 55 randomized controlled trials comprising 53, 268 patients that investigated use of beta blockers after MI. Mortality was significantly reduced 19% in patients receiving beta blockers [52]. The decrease in mortality after MI in persons treated with beta blockers was due to both a reduction in sudden cardiac death and recurrent MI [24-27, 53].

The Beta Blocker Heart Attack Trial was a double-blind, randomized study of 3, 290 patients after MI [53-55]. At 25-month follow-up, propranolol decreased sudden cardiac death by 28% in patients with complex VA and by 16% in patients without complex VA. Propranolol significantly reduced total mortality by 34% in patients aged 60 to 69 years ($p=0.01$) and insignificantly reduced total mortality by 19% in patients aged 30 to 59 years [53-55].

Beta blockers decrease complex VA including VT [55-57]. Beta blockers also increase VF threshold in animal models and have been found to decrease VF in patients with acute MI [58] A randomized, double-blind, placebo-controlled study of propranolol in high-risk survivors of acute MI at 12 Norwegian hospitals showed a 52% significant reduction in sudden cardiac death in patients treated with propranolol for 1 year [58].

Beta blockers decrease myocardial oxygen demand and myocardial ischemia, which may reduce the likelihood of VF. Stone et al [59] showed by 48-hour AECGs in 50 patients with stable angina pectoris that propranolol, but not diltiazem or nifedipine, caused a significant decrease in mean number of episodes of myocardial ischemia and in mean duration of myocardial ischemia compared with placebo. Beta blockers also decrease sympathetic tone, increase vagal tone, and stabilize cardiac membrane potentials which reduces the likelihood of VF. In addition, beta blockers are antithrombotic [60] and may prevent atherosclerotic plaque rupture [61].

In the retrospective study by Hallstrom et al [48] in 941 patients resuscitated from prehospital cardiac arrest attributed to VF, beta blockers were given to 28% of patients and no antiarrhythmic drug to 39% of patients. At 108-month follow-up, patients treated with beta

blockers had a significant 38% decreased incidence of death or recurrent cardiac arrest compared to patients treated with no antiarrhythmic [48].

Aronow et al [62] performed a prospective study in 245 persons with heart disease (64% with prior MI and 36% with hypertensive heart disease) and complex VA diagnosed by 24-hour AECGs and a LV ejection fraction ≥40%. Nonsustained VT occurred in 32% of patients. Silent myocardial ischemia occurred in 33% of patients. Of 245 patients, 123 were randomized to propranolol and 122 to no antiarrhythmic drug. Follow-up was 29 months. Propranolol was stopped because of adverse effects in 14 of 123 patients (11%).

Follow-up 24-hour AECGs were obtained at a median of 6 months in 91% of patients treated with propranolol and in 89% of patients treated with no antiarrhythmic drug [62]. Propranolol was significantly more effective than no antiarrhythmic drug in reducing VT >90% (71% versus 25% of patients) and in decreasing the average number of VPCs/hour >70% (71% versus 25% of patients) [62]. The prevalence of silent myocardial ischemia on follow-up 24-hour AECGs was insignificantly higher on no antiarrhythmic drug. However, silent ischemia was significantly abolished by propranolol, with 37% of patients with silent ischemia on their baseline 24-hour AECGs having no silent ischemia on their follow-up 24-hour AECGs [62].

Multivariate Cox regression analyses showed that propranolol caused a 47% significant reduction in sudden cardiac death, a 37% significant decrease in total cardiac death, and a 20% insignificant decrease in total death [62]. Univariate Cox regression analysis showed that among patients taking propranolol, suppression of complex VA caused a 33% insignificant reduction in sudden cardiac death, a 27% insignificant decrease in total cardiac death, and a 30% insignificant reduction in total death [63]. Among patients taking propranolol, abolition of silent myocardial ischemia caused a 70% significant decrease in sudden cardiac death, a 70% significant reduction in total cardiac death, and a 69% significant decrease in total death [63].

There was also a circadian distribution of sudden cardiac death or fatal MI with the peak incidence occurring from 6 AM to 12 PM (peak hour was 8 AM and a secondary peak occurred around 7 PM) in patients treated with no antiarrhythmic drug [64] Propranolol abolished this circadian distribution of sudden cardiac death or fatal MI [64]. In this study, propranolol markedly decreased the circadian variation of complex VA [65] and abolished the circadian variation of myocardial ischemia [66].

In a retrospective analysis of data from the CAST study, Kennedy et al [67] showed that 30% of patients with a LV ejection fraction ≤40% were receiving beta blockers. Patients on beta blockers had a significant decrease in all-cause mortality of 43% at 30 days, of 46% at 1 year, and of 33% at 2 years [67]. Patients treated with beta blockers had a significant reduction in arrhythmic death or cardiac arrest of 66% at 30 days, of 53% at 1 year, and of 36% at 2 years [67]. Multivariate analysis showed that beta blockers were an independent factor for decreasing arrhythmic death or cardiac arrest by 40%, for reducing all-cause mortality by 33%, and for decreasing new or worsened CHF by 32% [67].

ACE inhibitors have been shown to cause a significant reduction in complex VA in patients with CHF in some studies [68, 69] but not in other studies [70, 71]. ACE inhibitors have also been shown to reduce sudden cardiac death in some studies of patients with CHF [32, 72].

ACE inhibitors should be given to reduce total mortality in older and younger patients with CHF [30, 32, 72, 73], an anterior MI [31], an MI with a LV ejection fraction ≤40% [28, 29, 32], and in all patients with atherosclerotic cardiovascular disease [23, 33]. ACE inhibitors should be used to treat patients with CHF with abnormal LV ejection fraction [30, 32, 72, 73] or with normal LV ejection fraction [74, 75].

On the basis of available data, ACE inhibitors should be used to treat patients with VT or complex VA associated with CHF, an anterior MI, an MI with LV systolic dysfunction, or atherosclerotic cardiovascular disease if there are no contraindications to use of ACE inhibitors. Beta blockers should be used in addition to ACE inhibitors in treating these patients.

Class III antiarrhythmic drugs are potassium channel blockers which prolong repolarization manifested by an increase in QT interval on the electrocardiogram. These drugs suppress VA by increasing the refractory period. However, prolonging cardiac repolarization and refractory period can trigger afterdepolarizations and resultant torsade de pointes.

In the Survival With Oral d-Sotalol (SWORD) Trial, 3, 121 survivors of MI with a LV ejection fraction ≤40% were randomized to d-sotalol, a pure potassium channel blocker with no beta blocking activity, or to double-blind placebo [76]. At 148-day follow-up, mortality was 5.0% in patients treated with d-sotalol versus 3.1% in patients treated with placebo [76]. Presumed arrhythmic deaths accounted for the 77% increased mortality (relative risk = 1.77; 95% CI, 1.15 to 2.74) [76].

Studies comparing the effect of d, l-sotalol, a Class III antiarrhythmic drug with beta blocking activity, versus placebo or beta blockers in patients with VT or complex VA have not been performed. In a study of 1, 486 patients with prior MI, compared with placebo, d, l-sotalol did not reduce mortality in patients followed for 1 year [77].

In the Electrophysiologic Study versus Electrocardiographic Monitoring (ESVEM) study of 486 patients, Holter monitor-guided therapy significantly predicted antiarrhythmic drug efficacy more often than did the electrophysiologic study in patients with sustained VT or survivors of cardiac arrest (77% versus 45% of patients) [78]. However, there was no significant difference in the success of drug therapy selected by the two methods in preventing recurrences of ventricular tachyarrhythmias.

In the ESVEM study, d, l-sotalol was more effective than the other 6 antiarrhythmic drugs [imipramine, mexiletine, pirmenol, procainamide, propafenone, and quinidine] used in reducing recurrence of arrhythmia, death from arrhythmia, death from cardiac causes, and death from any cause [79]. However, 7 of 10 episodes of torsade de pointes during this study occurred in patients receiving d, l-sotalol [79]. In 481 patients with VT, d, l-sotalol caused torsade de pointes (12 patients) or an increase in VT episodes (11 patients) in 23 patients (4.9%) [80]. Women had a significantly higher risk for drug-induced VF. On the basis of available data, use of beta blockers is recommended over the use of d, l-sotalol in treating patients with VT or complex VA associated with heart disease.

Amiodarone is very effective in suppressing VT and complex VA associated with heart disease [81-83]. However, the incidence of adverse effects from amiodarone approaches 90% after 5 years of therapy [84]. In the Cardiac Arrest in Seattle: Conventional Versus Amiodarone Drug Evaluation study, the incidence of pulmonary toxicity was 10% at 2 years in patients receiving an amiodarone dose of 158 mg daily [81]. Amiodarone can also cause cardiac adverse effects, gastrointestinal adverse effects including hepatitis, hyperthyroidism, hypothyroidism, and neurologic, dermatologic, and ophthalmologic adverse effects.

A double-blind study randomized 674 patients with CHF and complex VA to amiodarone or placebo [82]. Compared with placebo, amiodarone significantly decreased the number of episodes of VT and the frequency of complex VA. Twenty-seven percent of patients discontinued amiodarone in this study. At 2-year follow-up, survival was not different in patients treated with amiodarone or placebo [82].

The Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT) randomized 1, 202 survivors of MI with nonsustained VT or complex VA to amiodarone or placebo [83] Early permanent discontinuation of amiodarone for reasons other than adverse events occurred in 36% of patients taking this drug [83]. At 1.8-year follow-up, amiodarone caused no significant reduction in mortality [83].

The European Myocardial Infarction Amiodarone Trial (EMIAT) randomized 1, 486 survivors of MI with a LV ejection fraction ≤40% to amiodarone or placebo [85]. Early permanent discontinuation of amiodarone occurred in 38.5% of patients taking this drug. At 21-month follow-up, mortality was similar in patients treated with amiodarone or with placebo [85].

In the Sudden Cardiac Death in Heart Failure Trial (SCD-HEFT), 2, 521 patients with New York Heart Association (NYHA) class II or III CHF due to ischemic or nonischemic heart disease, a LV ejection fraction of 35% or less, and a mean QRS duration on the resting ECG of 120 msec were randomized to placebo, amiodarone, or an automatic implantable cardioverter-defibrillator (AICD) [86]. At 45.5-month median follow-up, compared with placebo, amiodarone insignificantly increased mortality by 6% [86]. At 45.5-month median follow-up, compared with placebo, AICD therapy significantly reduced all-cause mortality by 23%, with an absolute reduction in mortality of 7.2% after 5 years [86].

Since amiodarone has not been found to reduce mortality in patients with VT or complex VA associated with MI or CHF and has a very high incidence of toxicity, beta blockers should be used rather than amiodarone in treating these patients. A meta-analysis of 10 randomized trials showed that the use of beta blockers significantly reduced 2-year mortality in patients receiving AICD therapy [87]. In a study of 965 patients with AICDs, at 32-month mean follow-up, use of beta blockers significantly reduced all-cause mortality by 46%, whereas use of amiodarone or sotalolol did not affect mortality [88]. During 33-month mean follow-up of 1, 038 patients with AICDs, use of beta blockers significantly reduced appropriate AICD shocks [89]. Use of amiodarone plus a beta blocker was not more effective than beta blocker therapy alone in reducing AICD shocks for any reason [89]. In this study, use of sotalol did not reduce appropriate AICD shocks [89].

4. Invasive intervention

If patients have life-threatening recurrent VT or VF resistant to antiarrhythmic drugs, invasive intervention should be performed. Patients with critical coronary artery stenosis and severe myocardial ischemia should undergo coronary artery bypass graft surgery to reduce mortality [90]. In the Coronary Artery Bypass Graft (CABG) Patch Trial, there was no evidence of improved survival among patients with CAD, LV ejection fraction <36%, and an abnormal signal-averaged electrocardiogram undergoing complete coronary revascularization in whom an AICD was implanted prophylactically at the time of elective coronary artery bypass graft surgery [91].

Surgical ablation of the arhythmogenic focus in patients with life-threatening ventricular tachyarrhythmias can be curative. This treatment includes aneurysectomy or infarctectomy and endocardial resection with or without adjunctive cryoablation based on activation mapping in the operating room [92-94]. However, the perioperative mortality rate is high. Endoaneurysmorrhaphy with a pericardial patch combined with mapping-guided subendocardial resection frequently cures recurrent VT with a low operative mortality and improvement of LV systolic function [95]. Radiofrequency catheter ablation of VT has been beneficial in the therapy of selected patients with arrhythmogenic foci of monomorphic VT [96-98]. Catheter ablation has been effectively used to treat patients with right ventricular outflow tract VT and LV fascicular VT. Prophylactic VT ablation should be considered before implantation of an AICD in patients with stable VT, prior MI, and reduced LV ejection fraction [99].

4.1. Automatic implantable cardioverter-defibrillator

However, the AICD is the most effective treatment for patients with life-threatening VT or VF. [93-110]. The Multicenter Automatic Defibrillator Implantation Trial (MADIT) randomized 196 patients, with a prior MI, a LV ejection fraction ≤35%, a documented episode of asymptomatic nonsustained VT, and inducible nonsuppressible ventricular tachyarrhythmia on electrophysiologic study to an AICD or conventional medical therapy [100]. At 27-month follow-up, patients receiving an AICD had a 54% significant reduction in mortality [100].

In the Antiarrhythmics versus Implantable Defibrillators (AVID) Trial, 1, 016 patients were randomized to an AICD or class III antiarrhythmic drug therapy [101]. Forty-five percent of patients had been resuscitated from near-fatal VF. The other 55% of patients had sustained VT with syncope or sustained VT with a LV ejection fraction ≤40% and symptoms suggesting severe hemodynamic compromise due to the arrhythmia (near-syncope, CHF, and angina pectoris). The 1-year survival was 89.3% for patients who had the AICD versus 82.3% for patients treated with drug therapy (39% reduction by AICD) [101]. The 2-year survival was 81.6% for patients who had the AICD versus 74.7% for patients treated with drug therapy (27% reduction by AICD) [101]. The 3-year survival was 75.4% for patients who had the AICD versus 64.1% for patients treated with drug therapy (31% reduction by AICD) [101].

The Canadian Implantable Defibrillator Study (CIDS) randomized 659 patients with VF, cardiac arrest, or hypotensive VT to an AICD or amiodarone therapy [102]. Cardiac arrhythmic mortality was 4.5% per year in patients treated with amiodarone versus 3% per year in patients treated with an AICD (risk reduction = 33%). Total mortality was 10.2% per year in patients treated with amiodarone versus 8.3% per year in patients treated with an AICD (risk reduction = 20%) [102]. In a subset of CIDS, at 5.6-year follow-up, 47% of patients treated with amiodarone and 27% of patients treated with an AICD had died [103]. Amiodarone caused adverse effects in 83% of patients receiving the drug [103].

The Cardiac Arrest Study Hamburg (CASH) randomized 230 patients surviving sudden cardiac death due to documented VT and/or VF to propafenone, metoprolol, amiodarone, or an AICD [104]. Propafenone was stopped after 11 months because mortality from sudden death and cardiac arrest recurrence was 23% in patients randomized to propafenone versus 0% in patients randomized to an AICD [104]. The 2-year mortality was 12.6% for 99 patients randomized to an AICD versus 19.6% for 189 patients randomized to amiodarone or metoprolol (37% reduction) [105].

The Multicenter Unsustained Tachycardia Trial randomized 704 patients with inducible, sustained ventricular tachyarrhythmias to 3 treatment groups [106]. Compared with electrophysiologically guided antiarrhythmic drug therapy, the 5-year total mortality was decreased 20% by an AICD, and the 5-year risk of cardiac arrest or death from an arrhythmia was reduced 76% by an AICD [106]. Neither total mortality incidence or rate of cardiac arrest or death from arrhythmia was lower in patients randomized to electrophysiologically guided therapy and treated with antiarrhythmic drugs than in patients randomized to no antiarrhythmic treatment [106].

MADIT II randomized 1, 232 patients with prior MI and a LV ejection fraction of ≤30% to an AICD or to conventional medical therapy [107]. At 20-month follow-up, compared with conventional medical therapy, the AICD reduced all-cause mortality 31% from 19.8% to 14.2% [107]. The effect of AICD therapy in improving survival was similar in patients stratified according to age, sex, LV ejection fraction, New York Heart Association class, and QRS interval [107].

In MADIT-II, the reduction in sudden cardiac death in patients treated with an AICD was significantly reduced by 68% in 574 patients aged <65 years, by 65% in 455 patients aged 65-74 years, and by 68% in 204 patients aged ≥75 years [108]. The median survival in 348 octogenarians treated with AICD therapy was >4years [109].

At 8-year follow-up in MADIT II, the cumulative probability of all-cause mortality was 49% for patients treated with an AICD versus 62% for patients not treated with an AICD [110]. AICD treatment caused a 34% reduction in mortality during treatment years 1-4 and a 26% reduction in mortality during years 5-8 [110].

After AICD implantation, 35 patients were randomized to treatment with metoprolol and 35 patients to treatment with d, l-sotalol [111]. VT recurrence was 17% at 1 year and 20% at 2 years for patients treated with metoprolol versus 43% at 1 year and 49% at 2 years for patients treated with d, l-sotalol. At 26-month follow-up, survival was 91% for patients treated

with metoprolol plus an AICD versus 83% for patients treated with d, l-sotalol plus an AICD [111]. In MADIT-II, use of higher doses of beta blockers in patients with ischemic heart disease and an AICD significantly reduced mortality by 56-58% compared with non-use of beta blockers [112]. These data favor using a beta blocker in patients with an AICD.

At 32-month mean follow-up of 965 patients, death occurred in 73 of 515 patients (13%) treated with beta blockers, in 84 of 494 patients (17%) treated with ACE inhibitors or angiotensin receptor blockers, in 56 of 402 patients (14%) treated with statins, in 40 of 227 patients (18%) treated with amiodarone, in 5 of 26 patients (19%) treated with sotalol, and in 64 of 265 patients (24%) treated with no beta blocker, ACE inhibitor, angiotensin receptor blocker, statin, amiodarone, or sotalol [88]. These data favor treating patients with AICDs with beta blockers, statins, and ACE inhibitors or angiotensin receptor blockers.

The American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines(Table 1) recommend that Class I indications for therapy with an AICD are 1) cardiac arrest due to VF or VT not due to a transient or a reversible cause; 2) spontaneous sustained VT; 3) syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiologic study when drug therapy is ineffective, not tolerated, or not preferred; ; 4) patients with prior MI at least 40 days previously with a LV ejection fraction less than 35% who are in NYHA class II or III; 5) patients with nonischemic dilated cardiomyopathy with a LV ejection fraction less than or equal to 35% who are in NYHA class II or III; 6) patients with prior MI at least 40 days previously with a LV ejection fraction less than 30% who are in NYHA class I; and 7) patients with nonsustained VT due to prior MI with a LV ejection fraction less than 40% and inducible VF or sustained VT at electrophysiological study [113].

1. Survivors of cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to diagnose the cause and to exclude completely reversible causes
2. Structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable
3. Syncope of undetermined etiology with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study
4. LV ejection fraction less than 35% due to prior MI at least 40 days previously and NYHA class II or III
5. Nonischemic dilated cardiomyopathy with LV ejection fraction less than or equal to 35% and NYHA class II or III
6. LV ejection fraction less than 30% due to prior myocardial infarction at least 40 days previously and NYHA class I
7. Nonsustained VT due to MI, LV ejection fraction less than 40%, and inducible VF or sustained VT at electrophysiological study

Table 1. Class I indications for Automatic Implantable Cardioverter-Defibrillator

Adapted from Epstein AE et al [113]

The 2009 updated ACCF/AHA guidelines for treatment of CHF (Table 2) recommend with a class I indication use of an AICD for 1) secondary prevention to increase survival in patients

with current or prior symptoms of heart failure and decreased LV ejection fraction who have a history of cardiac arrest, VF, or hemodynamically destabilizing VT; 2) primary prevention of sudden cardiac death to reduce mortality in patients with nonischemic dilated cardiomyopathy or CAD at least 40 days after MI, a LV ejection fraction less than or equal to 35%, and NYHA class II or III symptoms on optimal medical therapy, with expectation of survival with good functional status for more than 1 year; and 3) may be used in patients receiving cardiac resynchronization therapy (CRT) for NYHA class III or ambulatory class IV symptoms despite recommended optimal medical therapy [114, 115].

1. Secondary prevention to increase survival in patients with current or prior symptoms of heart failure and reduced LV ejection fraction with a history of cardiac arrest, VF, or hemodynamically destabilizing VT

2. Primary prevention of sudden cardiac death to reduce mortality in patients with nonischemic dilated cardiomyopathy or ischemic heart disease at least 40 days after MI, a LV ejection fraction less than or equal to 35%, and NYHA class II or III symptoms on optimal medical therapy, with expectation of survival with good functional status for more than 1 year

3. May be used in patients receiving cardiac resynchronization therapy for NYHA class III or ambulatory class IV symptoms despite recommended optimal medical therapy

Table 2. Class I Indications for Implantation of an Automatic Implantable Cardioverter-Defibrillator in Congestive Heart Failure

Adapted from Jessup M et al [114]

The ACC/AHA guidelines class IIa indications for treatment with an AICD are listed in Table 3 [113].

1. Unexplained syncope, significant LV dysfunction, and nonischemic dilated cardiomyopathy

2. Sustained VT and normal or near normal LV function

3. Hypertrophic cardiomyopathy with 1 or more major risk factor for SCD

4. Prevention of SCD in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy who have 1 or more risk factor for SCD

5. Reduction of SCD in patients with long-QT syndrome who are having syncope and/or VT while using beta blockers

6. Nonhospitalized patients awaiting cardiac transplantation

7. Brugada syndrome with syncope

8. Brugada syndrome with documented VT that has not resulted in cardiac arrest

9. Catecholaminergic polymorphic VT with syncope and/or documented sustained VT while using beta blockers

10. Cardiac sarcoidosis, giant cell myocarditis, or Chagas disease

Table 3. Class IIa Indications for Implantation of an Automatic Implantable Cardioverter-Defibrillator

Adapted from Epstein AE et al [113]

If the patient has no indication for pacing and a normal LV ejection fraction, CRT should not be performed. If the patient has no indication for pacing and a reduced LV ejection fraction, CRT should not be performed

An AICD may also be effective in preventing sudden death in patients with hypertrophic cardiomyopathy at high risk for sudden death [116] and in patients at high risk for sudden death because of a long QT interval or the Brugada syndrome [117]. An AICD may be useful in preventing sudden death in patients with syncope and ventricular tachyarrhythmias associated with poor LV ejection fraction, regardless of the result of the electrophysiologic study [118]. In addition, an AICD may be useful in survivors of VT or VF as a bridge to cardiac transplantation [119].

AICDs were implanted in 378 men and 95 women [120]. At 3.6-year follow-up, survival was 76% in patients who had an AICD because of cardiac arrest due to VF or VT not due to a transient or reversible cause, 85% in patients who had an AICD because of spontaneous sustained VT in association with structural heart disease, 92% in patients who had an AICD because of syncope of undetermined origin with clinically relevant, hemodynamically sustained VT or VF induced at electrophysiological study when drug therapy is ineffective, not tolerated, or not preferred, 84% in patients who had an AICD because of nonsustained VT with CAD, MI, LV dysfunction, and inducible VF or sustained VT at electrophysiological study that is not suppressible by a Class I antiarrhythmic drug, and 85% in all 473 patients [120].

AICDs are not effective in treating patients with LV dysfunction scheduled for elective CABG [91] or in patients who have had an acute MI within 40 days of the procedure [121, 122]. In patients receiving AICDs early after MI, factors associated with arrhythmias needing AICD therapy are also associated with a high risk of nonsudden death, negating the benefit of AICDs [123]. AICDs should also not be used to treat patients with NYHA class IV CHF despite optimal medical management or in patients with a life expectancy less than 1 year [114]

Of 209 patients with NYHA class III or IV heart failure treated with combined CRT-AICD therapy, appropriate cardioverter-defibrillator shocks occurred at 34-month follow-up in 22 of 121 patients (18%) on statins and in 30 of 88 patients (34%) not on statins [124]. Death occurred in 3 of 121 patients (2%) on statins and in 9 of 88 patients (10%) not on statins. Stepwise Cox regression analysis showed that significant independent prognostic factors for appropriate shocks were use of statins (risk ratio = 0.46), smoking (risk ratio = 3.5); and diabetes mellitus (risk ratio = 0.34) [124]. Significant independent prognostic factors for the time to mortality were use of statins (risk ratio = 0.05), use of digoxin (risk ratio = 4.2), hypertension (risk ratio = 14.2), diabetes mellitus (risk ratio = 4.3), and LV ejection fraction (risk ratio = 1.1) [124].

Of 529 patients with CHF and a reduced LV ejection fraction, 209 (40%) were treated with CRT plus an AICD and 320 (60%) with an AICD [125]. Mean follow-up was 34 months for both groups. Stepwise logistic regression analysis showed that significant independent vari-

ables for appropriate AICD shocks were statins (risk ratio = 0.35), smoking (risk ratio = 2.52), and digoxin (risk ratio = 1.92). Significant independent variables for time to deaths were use of CRT (risk ratio = 0.32), statins (risk ratio = 0.18), ACE inhibitors/angiotensin receptor blockers (ARBs) (risk ratio = 0.10), hypertension (risk ratio = 24.15), diabetes (risk ratio = 2.54), and age (risk ratio = 1.06) [125].

During 1243 days mean follow-up of 549 patients who had an AICD for CHF, 163 (30%) had appropriate AICD shocks, 71 (13%) had inappropriate AICD shocks, and 63 (12%) died [126]. Stepwise logistic regression analysis showed that significant independent prognostic factors for appropriate AICD shocks were smoking (odds ratio = 3.7) and statins (odds ratio = 0.54), for inappropriate AICD shocks were atrial fibrillation (odds ratio = 6.2) and statins (odds ratio = 0.52), and for time to mortality were age (hazard ratio = 1.08 per 1-year increase), ACE inhibitors or angiotensin receptor blockers ARBs (hazard ratio = 0.25), atrial fibrillation (hazard ratio = 4.1), right ventricular pacing (hazard ratio = 3.6), digoxin (hazard ratio = 2.9), hypertension (hazard ratio = 5.3), and statins (hazard ratio = 0.32) [126].

AICDs were implanted in 485 patients with ischemic cardiomyopathy and in 299 patients with nonischemic cardiomyopathy [127]. At 33-month follow-up, appropriate ICD shocks occurred in 179 of 485 patients (37%) with ischemic cardiomyopathy and in 93 of 299 patients (31%) with nonischemic cardiomyopathy. All-cause mortality occurred in 162 of 485 patients (33%) with ischemic cardiomyopathy and in 70 of 299 patients (23%) with nonischemic cardiomyopathy [127].

During implantatation and during 38-month follow-up of 1, 060 patients who had AICDs, complications occurred in 60 patients (5.7%) [128]. These complications consisted of fractured leads requiring lead revision in 36 patients (3.4%), lead infection requiring antibiotics in 5 patients (0.5%), device replacement because of malfunction in 5 patients (0.5%), repositioning of leads in 3 patients (0.3%), a hematoma at the time of implantation in 3 patients (0.3%), pneumothorax at the time of implantation in 2 patients (0.2%), repair of a defective generator in 1 patient (0.1%), replacement of the device because of atrophy of the skin over the device in 1 patient (0.1%), a transient ischemic attack because of atrial fibrillation developing during implantation in 1 patient (0.1%), device replacement because of a recall from Guidant in 1 patient (0.1%), pocket revision because of pain when lying on the side of the pacemaker in 1 patient (0.1%), and pacemaker infection in 1 patient (0.1%) [128]. A downloadable algorithm has been developed to reduce inappropriate shocks caused by fractures of implantable AICD leads [129].

Persistent atrial fibrillation is associated with appropriate shocks and with CHF in patients with LV dysfunction treated with an AICD [130]. One or more inappropriate AICD shocks occurred in 83 of 719 MADIT II patients (11.5%) and comprised 31.2% of 590 shocks [131]. Triggers for inappropriate shocks were atrial fibrillation (44%), supraventricular tachycardia (36%), and abnormal sensing (20%). Patients with inappropriate shocks had a 2.3 times increase in mortality [131].

In 1, 193 patients with combined CRT-AICD therapy, atrial tachycardia/atrial fibrillation lasting longer than 10 minutes occurred in 361 patients (30%) [132]. Device-detected atrial

tachycardia/atrial fibrillation was associated with a 2.16 times increased mortality at 13 months median follow-up [132].

Of 958 patients with an AICD, chronic kidney disease was a significant independent predictor of 1-year mortality [133]. The 1-year mortality was 1.8%, 5.3%, 9.0%, 22%, and 38% for stages 1, 2, 3, 4, and 5, respectively of renal function. [133].

Successful radiofrequecy ablation was performed in 22 of 84 patients with an AICD who had inappropriate shocks from atrial tachycardia, atrial flutter, or atrioventricular nodal reentrant tachycardia [134]. Ninety-five percent of 22 patients who underwent successful radiofrequency ablation for supraventricular tachycardia had no inappropriate AICD shocks at 21-month follow-up compared to 63% of patients with inappropriate shocks for supraventricular tachycardia who did not have radiofrequency ablation [134].

In patients with AICDs, compared to patients treated with ventricular backup pacing at a rate of 40/minute, patients treated with dual-chamber rate-responsive pacing at a rate of 70/minute (DDDR-70) had an increase in mortality [135, 136], worsening of LV ejection fraction [137], and an increase in new LV wall motion abnormality [137]. One reason why DDDR-70 pacing may increase mortality and worsen LV systolic function is that ventricular electrical activation proceeds from the right ventricular apex instead of through the existing conduction system.

In patients with AICDs and no indication for antibradycardia pacing, 22 of 80 patients (28%) treated with right ventricular pacing died at 45-month follow-up, and 8 of 81 patients (10%) treated with biventricular pacing died at 53-month follow-up [138]. At 23-month follow-up, the LV ejection fraction decreased from 36% to 30% in patients treated with right ventricular pacing and increased at 38-month follow-up from 35% to 40% in patients treated with biventricular pacing [138]. New LV wall motion abnormality developed at 23-month follow-up in 23 of 80 patients (29%) treated with right ventricular pacing and at 38-month follow-up in 7 of 81 patients (9%) treated with biventricular pacing [138]. On the basis of available data, patients with AICDs should be treated with biventricular pacing, not with DDDR-70 right ventricular pacing [135-138].

In the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) trial of 821 patients with nonischemic cardiomyopatyhy, 499 (61%) were treated with statins [139]. At 4-year follow-up, the cumulative probability of fast VT/VF or death was significantly reduced in patients treated with statins (11%) than in patients not treated with statins (19%) [139].

In the 1, 1820 patients in the MADIT-CRT trial, CRT -defibrillator therapy reduced first ventricular tachyarrhythmic events by 42% in patients with a left bundle branch block but did not reduce first ventricular tachyarrhythmic events in patients without left bundle branch block [140]. Recurrent ventricular tachyarrhythmic events were not reduced in patients with a left bundle branch block and were increased 3.62 times in patients without a left bundle branch block [140].

At 1.4-year follow-up of 1, 500 patients treated with an AICD for primary prevention, compared with conventional programming, programming the AICD for tachyarrhythmias of

200 beats per minute or higher was associated with a significant 79% reduction in inappropriate shocks or inappropriate antitachycardia pacing and a significant 55% reduction in all-cause mortality [141]. Compared with conventional programming, a prolonged delay in AICD therapy to 170 beats per minute or higher was associated with a significant 76% reduction in inappropriate shocks or inappropriate antitachycardia pacing and a significant 44% reduction in all-cause mortality [141].

At 1-year follow-up of 1, 902 patients treated with an AICD for primary or secondary prevention, use of a long-versus standard-detection interval caused a 42% significant reduction in antitachycardia pacing, a 23% insignificant reduction in appropriate shocks, a 45% significant reduction in inappropriate shocks, and a 13% insignificant reduction in mortality [142].

In a registry of 5, 399 AICD recipients for primary and secondary prevention, rates of appropriate shocks were similar among patients aged 18-49, 50-59, 60-69, 70-79, and ≥ 80 years [143]. There was no significant difference in mortality between clinical trial patients randomized to an AICD for primary prevention in the MADIT-II and SCD-HEFT trials and a similar group of clinical registry patient who received an AICD for primary prevention [144].

In patients with an AICD and a CRT-defibrillator, 3, 809 patients who survived a first shock were matched to 3, 630 patients without a shock [145]. Compared with no shock, mortality was significantly increased 1.65 times in those who received a shock for monomorphic VT, 2.1 times for those who received a shock for VF/polymorphic VT, and 161 times for those who received a shock for atrial fibrillation/atrial flutter [145]. Mortality was similar in those who received a shock for sinus tachycardia, supraventricular tachycardia, and noise/artefact oversensing compared to no shock [145].

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The author has no conflicts of interest.

References

[1] Fleg JL, Kennedy HL. Cardiac arrhythmia in a healthy elderly population. Detection by 24-hour ambulatory electrocardiography. Chest 1982;81:302-307.

[2] Aronow WS, Mercando AD, Epstein S. Prevalence of arrhythmias detected by 24-hour ambulatory electrocardiography and the value of antiarrhythmic therapy in elderly patients with unexplained syncope. Am J Cardiol 1992;70:408-410.

[3] Aronow WS, Epstein S, Mercando AD. Usefulness of complex ventricular arrhythmias detected by 24-hour ambulatory electrocardiogram and by electrocardiograms with one-minute rhythm strips in predicting new coronary events in elderly patients with and without heart disease. J Cardiovasc Technol 1991;10:21-25.

[4] Camm AJ, Evans KE, Ward DE, Martin A. The rhythm of the heart in active elderly subjects. Am Heart J 1980;99:598-603.

[5] Kantelip JP, Sage E, Duchene-Marullaz P. Findings on ambulatory electrocardiographic monitoring in subjects older than 80 years. Am J Cardiol 1986;57:398-401.

[6] Manolio TA, Furberg CD, Rautaharju PM, et al. Cardiac arrhythmias on 24-h ambulatory electrocardiography in older women and men: The Cardiovascular Health Study. J Am Coll Cardiol 1994;23:916-925.

[7] Aronow WS, Ahn C, Mercando A, et al. Prevalence and association of ventricular tachycardia and complex ventricular arrhythmias with new coronary events in older men and women with and without cardiovascular disease. J Gerontol: Med Sci 2002;57A:M178-M180.

[8] Aronow WS, Epstein S, Schwartz KS, Koenigsberg M. Prevalence of arrhythmias detected by ambulatory electrocardiographic monitoring and of abnormal left ventricular ejection fraction in persons older than 62 years in a long-term health care facility. Am J Cardiol 1987;59;368-369.

[9] Aronow WS, Epstein S, Schwartz KS, Koenigsberg M. Correlation of complex ventricular arrhythmias detected by ambulatory electrocardiographic monitoring with echocardiographic left ventricular hypertrophy in persons older than 62 years in a long-term health care facility. Am J Cardiol 1987;60:730-732.

[10] Aronow WS, Epstein S. Usefulness of silent ischemia, ventricular tachycardia, and complex ventricular arrhythmias in predicting new coronary events in elderly patients with coronary artery disease or systemic hypertension. Am J Cardiol 1990;65:511-522.

[11] Fleg JL, Kennedy HL. Long-term prognostic significance of ambulatory electrocardiographic findings in apparently healthy subjects ≥60 years of age. Am J Cardiol 1992;70:748-751.

[12] Fleg JL, Lakatta EG. Prevalence and prognosis of exercise-induced nonsustained ventricular tachycardia in apparently healthy volunteers. Am J Cardiol 1984;54:762-764.

[13] Busby MJ, Shefrin EA, Fleg JL. Prevalence and long-term significance of exercise-induced frequent or repetitive ventricular ectopic beats in apparently healthy volunteers. J Am Coll Cardiol 1989;14:1659-1665.

[14] Aronow WS, Epstein S, Koenigsberg M, Schwartz KS. Usefulness of echocardiographic abnormal left ventricular ejection fraction, paroxysmal ventricular tachycar-

dia, and complex ventricular arrhythmias in predicting new coronary events in patients over 62 years of age. Am J Cardiol 1988;61:1349-1351.

[15] Aronow WS, Epstein S, Koenigsberg M, Schwartz KS. Usefulness of echocardiographic left ventricular hypertrophy, ventricular tachycardia and complex ventricular arrhythmias in predicting ventricular fibrillation or sudden cardiac death in elderly patients. Am J Cardiol 1988;62:1124-1125.

[16] Moss AJ, Davis HT, DeCamilla J, Bayer LW. Ventricular ectopic beats and their relation to sudden and nonsudden death after myocardial infarction. Circulation 1979;60:998-1003.

[17] Bigger JT, Fleiss JL, Kleiger R, et al. The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. Circulation 1984;69:250-258.

[18] Mukharji J, Rude RE, Poole WK, et al. Risk factors for sudden death after acute myocardial infarction: Two-year follow-up. Am J Cardiol 1984;54:31-36.

[19] Kostis JB, Byington R, Friedman LM, et al. Prognostic significance of ventricular ectopic activity in survivors of acute myocardial infarction. J Am Coll Cardiol 1987;10:231-242.

[20] Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Br Med J 2002;324:71-86.

[21] Goldstein RE, Andrews M, Hall WJ, et al. Marked reduction in long-term cardiac deaths with aspirin after a coronary event. J Am Coll Cardiol 1996;28:326-330.

[22] Aronow WS, Ahn C. Reduction of coronary events with aspirin in older patients with prior myocardial infarction treated with and without statins. Heart Dis 2002;4:159-161.

[23] Smith SC Jr, Benjamin EJ,, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic cardiovascular disease: 2011 update. A guideline from the American Heart Association and American College of Cardiology Foundation. J Am Coll Cardiol 2011; 58:2432-2446.

[24] Hjalmarson A, Elmfeldt D, Herlitz J, et al. Effect on mortality of metoprolol in acute myocardial infarction. Lancet 1981;2:823-827.

[25] Gundersen T, Abrahamsen AM, Kjekshus J, et al. Timolol-related reduction in mortality and reinfarction in patients ages 65-75 years surviving acute myocardial infarction. Circulation 1982; 66:1179-1184.

[26] Pedersen TR for the Norwegian Multicentre Study Group. Six-year follow-up of the Norwegian Multicentre Study on Timolol after acute myocardial infarction. N Engl J Med 1985;313:1055-1058.

[27] Beta-Blocker Heart Attack Trial Research Group. A randomized trial of propranolol in patients with acute myocardial infarction. JAMA 1982; 247:1707-1714.

[28] Aronow WS, Ahn C, Kronzon I. Effect of beta blockers alone, of angiotensin-converting enzyme inhibitors alone, and of beta blockers plus angiotensin-converting enzyme inhibitors on new coronary events and on congestive heart failure in older persons with healed myocardial infarcts and asymptomatic left ventricular systolic dysfunction. Am J Cardiol 2001;88:1298-1300.

[29] Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the Survival and Ventricular Enlargement Trial. N Engl J Med 1992;327:669-677.

[30] The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. Lancet 1993;342:821-828.

[31] Ambrosioni E, Borghi C, Magnani B, for the Survival of Myocardial Infarction Long-Term Evaluation (SMILE) Study Investigators. The effect of the angiotensin-converting-enzyme inhibitor zofenopril on mortality and morbidity after anterior myocardial infarction. N Engl J Med 1995;332:80-85.

[32] Kober L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 1995;333:1670-1676.

[33] HOPE (Heart Outcomes Prevention Evaluation) Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med 2000;342:145-153.

[34] Miettinen TA, Pyorala K, Olsson AG, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris. Findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96:4211-4218.

[35] Lewis SJ, Moye LA, Sacks FM, et al. Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range. Results of the Cholesterol and Recurrent Events (CARE) Trial. Ann Intern Med 1998;129:681-689.

[36] The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998;339:1349-1357.

[37] Aronow WS, Ahn C. Incidence of new coronary events in older persons with prior myocardial infarction and serum low-density lipoprotein cholesterol ≥125 mg/dL treated with statins versus no lipid-lowering drug. Am J Cardiol. 2002;89:67-69.

[38] Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20, 536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002;360:7-22.

[39] Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 2002:360:1623-1630.

[40] Stone NJ, Robinson J, Lichtenstein AH, et al. ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition for Women with Heart Disease. J Am Coll Cardiol 2013; published online November 12, 2013.

[41] Frishman WH Aronow WS, Cheng-Lai A. Cardiovascular drug therapy in the elderly. In: Aronow WS, Fleg J, Rich MW, eds. Cardiovascular Disease in the Elderly, fourth edition, New York City: Informa Healthcare 2008:99-135

[42] IMPACT Research Group. International Mexiletine and Placebo Antiarrhythmic Coronary Trial: I. Report on arrhythmia and other findings. J Am Coll Cardiol 1984;4:1148-1163

[43] The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report. Effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. N Engl J Med 1989;321:406-412.

[44] Akiyama T, Pawitan Y, Campbell WB, et al. Effects of advancing age on the efficacy and side effects of antiarrhythmic drugs in post-myocardial infarction patients with ventricular arrhythmias. J Am Geriatr Soc 1992;40:666-672.

[45] The Cardiac Arrhythmia Suppression Trial II Investigators. Effect of the antiarrhythmic agent moricizine on survival after myocardial infarction. N Engl J Med 1992;327:227-233.

[46] Aronow WS, Mercando AD, Epstein S, Kronzon I. Effect of quinidine or procainamide versus no antiarrhythmic drug on sudden cardiac death, total cardiac death, and total death in elderly patients with heart disease and complex ventricular arrhythmias. Am J. Cardiol 1990;66:423-428.

[47] Moosvi AR, Goldstein S, VanderBrug Medendorp S, et al. Effect of empiric antiarrhythmic therapy in resuscitated out-of-hospital cardiac arrest victims with coronary artery disease. Am J Cardiol 1990;65:1192-1197.

[48] Hallstrom AP, Cobb LA, Hui Yu B, et al. An antiarrhythmic drug experience in 941 patients resuscitated from an initial cardiac arrest between 1970 and 1985. Am J Cardiol 1991;68:1025-1031.

[49] Coplen SE, Antmann EM, Berlin JA, et al. Efficacy and safety of quinidine therapy for maintenance of sinus rhythm after cardioversion: A meta-analysis of randomized control trials. Circulation 1990;82:1106-1116.

[50] Flaker GC, Blackshear JL, McBride R, et al. Antiarrhythmic drug therapy and cardiac mortality in atrial fibrillation. J Am Coll Cardiol 1992;20:527-532.

[51] Morganroth J, Goin JE. Quinidine-related mortalitiy in the short-to-medium term treatment of ventricular arrhythmias. A meta-analysis. Circulation 1991;84:1977-1983.

[52] Teo KK, Yusuf S, Furberg CD. Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction. An overview of results from randomized controlled trials. JAMA 1993;270:1589-1595.

[53] Hawkins CM, Richardson DW, Vokonas PS, for the BHAT Research Group. Effect of propranolol in reducing mortality in older myocardial infarction patients. The Beta-Blocker Heart Attack Trial experience. Circulation 1983;67[suppl I]:I-94-I-97.

[54] Friedman LM, Byington RP, Capone RJ, et al. Effect of propranolol in patients with myocardial infarction and ventricular arrhythmia. J Am Coll Cardiol 1986;7:1-8.

[55] Lichstein E, Morganroth J, Harrist R, et al. Effect of propranolol on ventricular arrhythmia. The Beta-Blocker Heart Attack Trial experience. Circulation 1983;67[suppl I]:I-5-I-10.

[56] Hansteen V. Beta blockade after myocardial infarction: The Norwegian Propranolol Study in high-risk patients. Circulation 1983;67[suppl I]:I-57-I-60.

[57] de Soyza N, Shapiro W, Chandraratna PAN, et al. Acebutolol for ventricular arrythmia: A randomized, placebo-controlled, double-blind multicenter study. Circulation 1982;65:1129-1133.

[58] Norris RM, Barnaby PF, Brown MA, et al. Prevention of ventricular fibrillation during acute myocardial infarction by intravenous propranolol. Lancet 1984;2:883-886.

[59] Stone PH, Gibson RS, Glasser SP, et al. Comparison of propranolol, diltiazem, and nifedipine in the treatment of ambulatory ischemia in patients with stable angina. Differential effects on ambulatory ischemia, exercise performance, and anginal symptoms. Circulation 1990;82:1962-1972.

[60] Weksler BB, Gillick M, Pink J. Effects of propranolol on platelet function. Blood 1977;49:185-196.

[61] Frishman WH, Lazar EJ. Reduction of mortality, sudden death and non-fatal infarction with beta-adrenergic blockers in survivors of acute myocardial infarction: A new

hypothesis regarding the cardioprotective action of beta-adrenergic blockade. Am J Cardiol 1990;66(suppl):66G-70G.

[62] Aronow WS, Ahn C, Mercando AD, et al. Effect of propranolol versus no antiarrhythmic drug on sudden cardiac death, total cardiac death, and total death in patients ≥62 years of age with heart disease, complex ventricular arrhythmias, and left ventricular ejection fraction ≥40%. Am J Cardiol 1994;74:267-270.

[63] Aronow WS, Ahn C, Mercando AD, et al. Decrease of mortality by propranolol in patients with heart disease and complex ventricular arrhythmias is more an anti-ischemic than an antiarrhythmic effect. Am J Cardiol 1994;74:613-615.

[64] Aronow WS, Ahn C, Mercando AD, Epstein S. Circadian variation of sudden cardiac death or fatal myocardial infarction is abolished by propranolol in patients with heart disease and complex ventricular arrhythmias. Am J Cardiol 1994;74:819-821.

[65] Aronow WS, Ahn C, Mercando AD, Epstein S. Effect of propranolol on circadian variation of ventricular arrhythmias in elderly patients with heart disease and complex ventricular arrhythmias. Am J Cardiol 1995;75:514-516.

[66] Aronow WS, Ahn C, Mercando AD, Epstein S. Effect of propranolol on circadian variation of myocardial ischemia in elderly patients with heart disease and complex ventricular arrhythmias. Am J Cardiol 1995;75:837-839.

[67] Kennedy HL, Brooks MM, Barker AH, et al. Beta-blocker therapy in the Cardiac Arrhythmia Suppression Trial. Am J Cardiol 1994;74:674-680.

[68] Webster MW, Fitzpatrick MA, Nicholls MG, et al. Effect of enalapril on ventricular arrhythmias in congestive heart failure. Am J Cardiol 1985;56:566-569.

[69] Fletcher RD, Cintron GB, Johnson G, et al. Enalapril decreases prevalence of ventricular tachycardia in patients with chronic congestive heart failure. Circulation 1993;87[suppl VI]:VI-49-VI-55.

[70] Pratt CM, Gardner M, Pepine C, et al. Lack of long-term ventricular arrhythmia reduction by enalapril in heart failure. Am J Cardiol 1995;75:1244-1249.

[71] Aronow WS, Mercando AD, Epstein S. Effect of benazepril on complex ventricular arrhythmias in older patients with congestive heart failure, prior myocardial infarction, and normal left ventricular ejection fraction. Am J Cardiol 1998;81:1368-1370.

[72] Cohn JN, Johnson G, Ziesche S, et al. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. N Engl J Med 1991;325:303-310.

[73] Garg R, Yusuf S, for the Collaborative Group on ACE Inhibitor Trials. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. JAMA 1995;273:1450-1456.

[74] Aronow WS, Kronzon I. Effect of enalapril on congestive heart failure treated with diuretics in elderly patients with prior myocardial infarction and normal left ventricular ejection fraction. Am J Cardiol 1993;71:602-604.

[75] Philbin EF, Rocco TA Jr, Lindenmuth NW, et al. Systolic versus diastolic heart failure in community practice: clinical features, outcomes, and the use of angiotensin-converting enzyme inhibitors. Am J Med 2000;109:605-613.

[76] Waldo AL, Camm AJ, deRuyter H, et al. Effect of d-sotalol on mortality in patients with left ventricular dysfunction after recent and remote myocardial infarction. Lancet 1996;348:7-12.

[77] Julian DJ, Prescott RJ, Jackson FS, Szekely P. Controlled trial of sotalol for one year after myocardial infarction. Lancet 1982;1:1142-1147.

[78] Mason JW for the Electrophysiologic Study versus Electrocardiographic Monitoring Investigators. A comparison of electrophysiologic testing with Holter monitoring to predict antiarrhythmic-drug efficacy for ventricular tachyarrhythmias. N Engl J Med 1993;329:445-451.

[79] Mason JW for the Electrophysiologic Study versus Electrocardiographic Monitoring Investigators. A comparison of seven antiarrhythmic drugs in patients with ventricular tachyarrhythmias. N Engl J Med 1993;329:452-458.

[80] Kehoe RF, MacNeil DJ, Zheutlin TA, et al. Safety and efficacy of oral sotalol for sustained ventricular tachyarrhythmias refractory to other antiarrhythmic agents. Am J Cardiol 1993;72:56A-66A.

[81] Greene HL for the CASCADE Investigators. The CASCADE study. Randomized antiarrhythmic drug therapy in survivors of cardiac arrest in Seattle. Am J Cardiol 1993;72:70F-74F.

[82] Singh SN, Fletcher RD, Fisher SG, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. N Engl J Med 1995;333:77-82.

[83] Cairns JA, Connolly SJ, Roberts R, et al. Randomised trial of outcome after myocardial infarction in patients with frequent or repetitive ventricular premature depolarisations: CAMIAT. Lancet 1997;349:675-682.

[84] Herre J, Sauve M, Malone P, et al. Long-term results of amiodarone therapy in patients with recurrent sustained ventricular tachycardia or ventricular fibrillation. J Am Coll Cardiol 1989;13:442-449.

[85] Julian DG, Camm AJ, Frangin G, et al. Randomised trial of effect of amiodarone on mortality in patients with left-ventricular dysfunction after recent myocardial infarction: EMIAT. Lancet 1997;349:667-674.

[86] Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225-237.

[87] Makikallio TH, Huikuri HV. Association between usage of beta-blocking medication and benefit from implantable cardioverter therapy. Am J Cardiol 2006;98:1245-1247.

[88] Lai HM, Aronow WS, Kruger A, Dersai H, Amin H, Frishman WH, et al. Effect of beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins on mortality in patients with implantable cardioverter-defibrillators. Am J Cardiol 2008; 102:77-78.

[89] Kruger A, Aronow WS, Lai H, Desai H, Singla A, Frishman WH, et al. Prevalence of appropriate cardioverter-defibrillator shocks in 1038 consecutive patients with implantable cardioverter-defibrillators. Am J Therap 2009; 16:323-325.

[90] O'Rourke RA. Role of myocardial revascularization in sudden cardiac death. Circulation 1992;85(suppl I):I-112-I-117.

[91] Bigger JT Jr, for the Coronary Artery Bypass Graft (CABG) Patch Trial Investigators. Prophylactic use of implanted cardiac defibrillators in patients at high risk for ventricular arrhythmias after coronary artery bypass graft surgery. N Engl J Med 1997;337:1569-1575.

[92] Platia EV, Griffith LSC, Watkins L Jr, et al. Treatment of malignant ventricular arrhythmias with endocardial resection and implantation of the automatic cardioverter-defibrillator. N Engl J Med 1986;314:213-216.

[93] Tresch DD, Platia EV, Guarnieri T, et al. Refractory symptomatic ventricular tachycardia and venricular fibrillation in elderly patients. Am J Med 1987;83:399-404.

[94] Tresch DD, Troup PJ, Thakur RK, et al. Comparison of efficacy of automatic implantable cardioverter defibrillator in patients older and younger than 65 years of age. Am J Med 1991;90:717-724.

[95] Rastegar H, Link MS, Foote CB, et al. Perioperative and long-term results with mapping-guided subendocardial resection and left ventricular endoaneurysmorrhaphy. Circulation 1996;94:1041-1048.

[96] Morady F, Harvey M, Kalbfleisch SJ, et al. Radiofrequency catheter ablation of ventricular tachycardia in patients with coronary artery disease. Circulation 1993;87:363-372.

[97] Gonska B-D, Cao K, Schaumann A, et al. Catheter ablation of ventricular tachycardia in 136 patients with coronary artery disease: Results and long-term follow-up. J Am Coll Cardiol 1994;24:1506-1514.

[98] Channamsetty V, Aronow WS, Sorbera C, et al. Efficacy of radiofrequency catheter ablation in treatment of elderly patients with supraventricular tachyarrhythmias and ventricular tachycardia. Am J Therap 2006; 13: 513-515.

[99] Kuck K-H, Schaumann A, Eckardt L, et al. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. Lancet 2010; 375: 31-40.

[100] Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med 1996;335:1933-1940.

[101] The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med 1997;337:1576-1583.

[102] Roy D, Green M, Talajic M, et al. Mode of death in the Canadian Implantable Defibrillator Study (CIDS) (abstract). Circulation 1998;98(suppl I):1-495.

[103] Bokhari F, Newman D, Greene M, et al. Long-term comparison of the implantable cardioverter defibrillator versus amiodarone. Eleven-year follow-up of a subset of patients in the Canadian Implantable Defibrillator Study CIDS. Circulation 2004;110:112-116.

[104] Siebels J, Cappato R, Ruppel R, et al. Preliminary results of the Cardiac Arrest Study Hamburg (CASH). Am J Cardiol 1993;72:109F-113F.

[105] Cappato R, Siebels J, Kuck KH. Value of programmed electrical stimulation to predict clinical outcome in the Cardiac Arrest Study Hamburg (CASH) (abstract). Circulation 1998;98(suppl I):I-495-I-496.

[106] Buxton AE, Lee KL, Fisher JD, et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. N Engl J Med 1999;341:1882-1890.

[107] Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877-883.

[108] Goldenberg I, Moss AJ. Treatment of arrhythmias and use of implantable cardioverter-defibrillators to improve survival in elderly patients with cardiac disease. In Aronow WS (ed): Clinics in Geriatric Medicine on Heart Failure, Philadelphia, Elsevier, 2007; 23:205-219.

[109] Kaplan BA, Epstein LM, Albert CM, Stevenson WG. Survival in octogenarians receiving implantable defibrillators. Am Heart J 2006;152:714-719.

[110] Goldenberg I, Gillespie J, Moss AJ, et al. Long-term benefit of primary prevention with an implantable cardioverter-defibrillator. An extended 8-year follow-up study of the MulticenterAutomatic Defibrillator Implantation Trial II. Circulation 2010; 122: 1265-1271.

[111] Seidl K, Hauer B, Schwick NG, et al. Comparison of metoprolol and sotalol in preventing ventricular tachyarrhythmias after the implantation of a cardioverter/defibrillator. Am J Cardiol 1998;82:744-748.

[112] Brodine WN, Tung RT, Lee JK, et al. Effects of beta-blockers on implantable cardioverter defibrillator therapy and survival in the patients with ischemic cardiomyopathy (from the Multicenter Automatic Defibrillator Implantation Trial-II. Am J Cardiol 2005;96:691-695.

[113] Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. ACC/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: Executive Summary. A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices). Developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. J Am Coll Cardiol 2008; 51:2085-2105

[114] Jessup M, Abraham WT, Casey DE, et al. 2009 focused update: ACCF/AHA guidelines for the diagnosis and management of heart failure in adults. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the International Society for Heart and Lung Transplantation. J Am Coll Cardiol 2009; 53: 1343-1382..

[115] Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Eng J Med 2004; 350: 2140-2150.

[116] Maron BJ, Shen W-K, Link MS, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. N Engl J Med 2000;342:365-373.

[117] Brugada P, Brugada R, Brugada J, Geelen P. Use of the prophylactic implantable cardioverter defibrillator for patients with normal hearts. Am J Cardiol 1999;83:98D-100D.

[118] LeLorier P, Krahn AD, Klein GJ, et al. Comparison of patients with syncope with left ventricular dysfunction and negative electrophysiologic testing to cardiac arrest survivors and patients with syncope and preserved left ventricular function and impact of an implantable defibrillator. Am J Cardiol 2002;90:77-79.

[119] Lorga-Filho A,, Geelen P, Vanderheyden M, et al. Early benefit of implantable cardioverter defibrillator therapy in patients waiting for cardiac transplantation. Pacing Clin Electrophysiol 1998;21:1747-1751.

[120] Aronow WS, Sorbera C, Chagarlamudi A, et al. Indications for and long-term survival in patients with automatic implantable cardioverter-defibrillators. Cardiol Rev 2005;13:50-51.

[121] Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. N Engl J Med 2004;351:2481-2488.

[122] Steinbeck G, Andresen D, Seidl K, et al. Defibrillator implantation early after myocardial infarction. N Engl J Med 2009; 361: 1427-1436.

[123] Dorian P, Hohnloser SH, Thorpe KE, et al. Mechanisms underlying the lack of effect of implantable cardioverter-defibrillator therapy on mortality in hgh-risk patients with recent myocardial infarction. Insights from the Defibrillation in Acute Myocardial Infarction trial (DINAMIT). Circulation 2010; 122: 2645-2652.

[124] Desai H, Aronow WS, Tsai FS, et al. Statins reduce appropriate cardioverter-defibrillator shocks and mortality in patients with heart failure and combined cardiac resynchronization and implantable cardioverter-defibrillator therapy. J Cardiovasc Pharmacol Therap 2009; 14:176-179.

[125] Desai H, Aronow WS, Ahn C, Tsai FS, et al. Incidence of appropriate cardioverter-defibrillator shocks and mortality in patients with heart failure treated with combined cardiac resynchronization therapy plus implantable cardioverter-defibrillator therapy versus implantable cardioverter-defibrillator therapy. J Cardiovasc Pharmacol Therap 2010; 15:37-40.

[126] Desai H, Aronow WS, Ahn C, Gandhi K, Hussain S, Lai HM, et al. Risk factors for appropriate cardioverter-shocks, inappropriate cardioverter shocks, and time to mortality in 549 patients with heart failure. Am J Cardiol 2010; 105:1336-1338.

[127] Gandhi K, Aronow WS, Desai H, Amin H, Lai HM, Frishman WH, et al. Incidence of appropriate cardioverter-defibrillator shocks and mortality in patients with implantable cardioverter-defibrillators with ischemic cardiomyopathy versus nonischemic cardiomyopathy at 33-month follow-up. Arch Med Sci 2010; 6:900-903.

[128] Tsai F, Aronow WS, Devabhaktuni S, Desai H, Kruger A, Lai HM, et al. Prevalence of complications during implantation and during 38-month follow-up of 1060 consecutive patients with implantable cardioverterr-defibrillators. Am J Therap 2010; 17: e8-e10.

[129] Swerdlow CD, Gunderson BD, Ousdigian KT, Abeyatne A, Stadler RW, Gillberg JM, et al. Downloadable algorithm to reduce inappropriate shocks caused by fractures of implantable cardioverter-defibrillator leads. Circulation 2008; 118: 2122-2129.

[130] Rienstra M, Smit MD, Nieuwland W, et al. Persistent atrial fibrillation is associated with appropriate shocks and heart failure in patients with left ventricular dysfunction treated with an implantable cardioverter defibrillator. Am Heart J 2007; 153: 120-126.

[131] Daubert JP, Zareba W, Cannom DS, et al. Inappropriate implantable cardioverter-defibrillator shocks in MADIT II. Frequency, mechanisms, predictors, and survival impact. J Am Coll Cardiol 2008; 51: 1357-1365.

[132] Santini M, Gasparini M, Landolina M, et al. Device-detected atrial tachyarrhythmias predict adverse outcome in real-world patients with implantable biventricular defibrillators. J Am Coll Cardiol 2011; 57: 167-172.

[133] Hager CS, Jain S, Blackwell J, et al. Effect of renal function on survival after implantable cardioverter defibrillator placement. Am J Cardiol 2010; 106: 1297-1300.

[134] Mainigi SK, Almuti K, Figueredo VM, et al. Usefulness of radiofrequency ablation of supraventricular tachycardia to decrease inappropriate shocks from implantable cardioverter-defibrillators. Am J Cardiol 2012; 109: 231-237

[135] The DAVID Trial Investigators. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator. The Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA 2002;288:3115-3123.

[136] Sukhija R, Aronow WS, Sorbera C, et al. Patients, mean age 70 years, with dual-chamber rate-responsive pacing (DDDR-70) have a higher mortality than patients with backup ventricular pacing (VVI-40) at 3.7-year follow-up. J Gerontol: Med Sci 2005;60A:M603-M604.

[137] Sukhija R, Aronow WS, Sorbera C, et al. Left ventricular ejection fraction and prevalence of new left ventricular wall motion abnormality at long-term follow-up in patients treated with dual-chamber rate-responsive pacing at a rate of 70/minute versus backup ventricular pacing at a rate of 40/minute. Am J Cardiol 2005;96:412-413.

[138] Sukhija R, Aronow WS, Sorbera C, et al. Mortality, left ventricular ejection fraction, and prevalence of new left ventricular wall motion abnormality in patients with implantable cardioverter-defibrillators treated with biventricular pacing versus right venricular pacing. Am J Therap 2007;14:328-330.

[139] Buber J, Goldenberg I, Moss AJ, et al. Reduction in life-threatening ventricular tachyarrhythmias in statin-treated patients with nonischemic cardiomyopathy enrolled in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy). J Am Coll Cardiol 2012; 60: 749-755.

[140] Ouellet G, Huang DT, Moss AJ, et al. Effect of cardiac resynchronization therapy on the risk of first and recurrent ventricular tachyarrhythmic events in MADIT-CRT. J Am Coll Cardiol 2012; 60: 1809-1816..

[141] Moss AJ, Schuger C, Beck CA, et al. Reduction in inappropriate therapy and mortality through ICD programming. N Engl J Med 2012; 367: 2275-2283.

[142] Gasparini M, Proclemer A, Klersy C, et al. Effect of long-detection interval vs standard-detection interval for implantable cardioverter-defibrillators on antitachycardia

pacing and shock delivery. The ADVANCE III randomized clinical trial. JAMA 2013; 309: 1903-1911.

[143] Yung D, Birnie D, Dorian P, et al. Survival after implantable cardioverter-defibrillator implantation in the elderly. Circulation 2013; 127: 2383-2392.

[144] Al-Khatib SM, Hellkamp A, Bardy GH, et al. Survival of patients receiving a primary prevention implantable cardioverter-defibrillator in clinical practice vs clinical trials. JAMA 2013; 309: 55-62.

[145] Powel BD, Saxon LA, Boehmer JP, et al. Survival after shock therapy in implantable cardioverter-defibrillator and cardiac resynchronization therapy-defibrillator recipients according to rhythm shocked. The ALTITUDE Survival by Rhythm Study. J Am Coll Cardiol 2013; 62: 1674-1679.

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