JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 64, NO. 11, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.04.008

EXPERT CONSENSUS STATEMENT

HRS/ACC/AHA Expert Consensus Statement on the Use of Implantable Cardioverter-Defibrillator Therapy in Patients Who Are Not Included or Not Well Represented in Clinical Trials

Developed in partnership with and endorsed by the American College of Cardiology (ACC) and the American Heart Association (AHA); and in collaboration with and endorsed by the Heart Failure Society of America (HFSA) and the Society of Thoracic Surgeons (STS)

Endorsed by the European Heart Rhythm Association (EHRA), the Asia Pacific Heart Rhythm Society (APHRS) and the Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLAECE)-Latin American Society of Cardiac Pacing and Electrophysiology

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The American College of Cardiology requests that this document be cited as follows: Kusumoto FM, Calkins H, Boehmer J, Buxton AE, Chung MK, Gold MR, Hohnloser SH, Indik J, Lee R, Mehra MR, Menon V, Page RL, Shen W-K, Slotwiner DJ, Warner Stevenson L, Varosy PD, Welikovitch L. HRS/ACC/AHA expert consensus statement on the use of implantable cardioverter-defibrillator therapy in patients who are not included or not well represented in clinical trials. J Am Coll Cardiol 2014;64:1143-77.

This article is copublished in *Heart Rhythm* and *Circulation*.

JACC VOL. 64, NO. 11, 2014
SEPTEMBER 16, 2014:1143–77

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1. INTRODUCTION

The implantable cardioverter defibrillator (ICD) has emerged as an important treatment option for selected patients who are at risk of sudden cardiac death. Randomized trials have consistently shown that ICD implantation reduces mortality in patients with heart failure and reduced left ventricular function, as well as in patients who have suffered a cardiac arrest (1–3). Recommendations on the use of the ICD in clinical practice have been provided in four important guideline documents sponsored by the American College of Cardiology (ACC), the American Heart Association (AHA), Heart Rhythm Society (HRS), and the European Society of Cardiology (ESC) (4–7). For each indication for ICD therapy, both a Class of indication (I, II, or III) and level of evidence for the indication (A, B, or C) are provided. To ensure that recommendations are evidence-based, Class I recommendations are typically based on the results of prospective randomized clinical trials. For example, in the ACC/AHA/HRS 2012 Focused Update of the ACC/AHA/HRS 2008 Guidelines on Device-Based Therapy, no new recommendations on the indications for ICD therapy were made, with the important exception of ICDs that also provide cardiac resynchronization therapy (CRT-D) (8). The lack of new recommendations reflects the fact that clinical trials over this period of time have focused on studying the effectiveness of ICDs that provide CRT therapy and not on the outcomes of non-CRT defibrillators. Randomized clinical trials study the effects of a particular treatment on a carefully selected and relatively homogeneous group of patients who meet specific inclusion and exclusion criteria for a particular clinical trial. Consistent with this approach, the indications for ICD therapy developed in the various guideline statements are limited to the specific populations of patients who participated in these clinical trials. Although the resulting guidelines are of great value, clinicians are often asked to make decisions regarding ICD therapy in patient populations who were not included or who were poorly represented in prior clinical trials. For these patients, there are no specific indications for ICD therapy. The purpose of this consensus statement is to provide clinicians with guidance on the use of ICD therapy in the management of some common populations of patients who are not represented in clinical trials and who therefore are not specifically included in the various guidelines that provide indications for ICD therapy. However, recommendations made in this document cannot account for all the nuances of clinical medicine and cannot replace careful clinical judgment for the care of an individual patient.

This document is not meant to be a comprehensive guideline on a specific clinical subject. Recommendations are not given a Class recommendation; instead, phrases such as “is recommended,” “can be useful,” “can be considered,” and “is not recommended” are used. In addition, no levels of evidence are provided because there are no randomized controlled trials that have been specifically designed to address the clinical conditions posed by this document. The recommendations are largely based on subgroup analysis of randomized clinical trials, retrospective studies, analyses of large registries, and expert

opinion. Similarly, this document does not use the same methodology as an Appropriate Use Criteria document (9).

For this consensus document, the writing group evaluated the available data on four important situations for which ICD therapy might be beneficial in selected populations that were not consistently included in randomized clinical trials: 1) use of an ICD in patients with an abnormal troponin that is not due to a myocardial infarction (MI), 2) use of an ICD within 40 days after a myocardial infarction, 3) use of an ICD within the first 90 days after revascularization, and 4) use of an ICD in the first 9 months after initial diagnosis of nonischemic cardiomyopathy. In addition, the writing group evaluated the utility of an atrial lead in a patient requiring ICD therapy without cardiac resynchronization therapy. The members of the writing group performed a comprehensive literature search, and then developed a series of recommendations with an explanation of the reasoning and research used to make each recommendation. Initial recommendations and alternatives were discussed and edited by the entire group. Final recommendations were sent to the entire group for anonymous voting. All recommendations presented in this document were agreed upon by at least 80% of the members of the writing group. The writing group members were selected by the following societies: Heart Rhythm Society, American College of Cardiology, American Heart Association, Heart Failure Society of America, and the Society of Thoracic Surgeons. Members of the writing group are from the United States, Canada, and Europe, and were selected as leaders in their fields with the majority of the writing group having no significant relationships with the medical device industry. All members of the writing committee were allowed to vote unless a significant relationship with industry was identified by the individual or the co-chairs.

2. CURRENT GUIDELINES THAT ADDRESS ICD USE

Several Guidelines have been published that evaluate the use of ICDs in various clinical situations (**Table 1**) (4–7). Although generally similar, there are some differences among the various documents because each group evaluated ICD implantation from a slightly different perspective. For example, three of the guidelines, the ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death, the ACC/AHA/HRS 2008 Guidelines on Device-Based Therapy, and the 2009 ACC/AHA Focused Update of the 2005 Heart Failure Guidelines, addressed the use of non-CRT ICD therapy in patients with heart failure (4–6). The 2008 Guidelines on Device-Based Therapy and the 2009 Focused Update of the 2005 Heart Failure Guidelines provide specific ejection fraction cut-offs that parallel the values used in randomized clinical trials (4,5). In the text discussing the basis for the recommendations, the 2008 Guidelines on Device-Based Therapies noted that ejection fraction determination could be variable and suggested that clinicians rely on the most clinically accurate modality at their specific institution (5). Using a slightly different approach, the 2006 Guidelines on Ventricular Arrhythmias acknowledged the variability of many measures for ejection fraction and provided a range in the actual recommendations that provides increased flexibility at the cost of potential overuse (7). Clearly, the trend has been an emphasis on the incorporation of results from randomized clinical trials into the recommendations made by Guidelines documents.

3. RANDOMIZED CONTROLLED TRIALS OF ICD THERAPY FOR PRIMARY PREVENTION OF SUDDEN CARDIAC DEATH

Seven large randomized trials have evaluated the use of ICDs in patients at risk of sudden cardiac death due to heart failure or left ventricular dysfunction in the setting of prior MI (**Table 2** and **Figure 1**) (1,2,10–12,14–16). Each of the trials evaluated slightly different patient groups, and all of the trials, with the exception of the Coronary Artery Bypass Graft (CABG)-Patch trial, identified a patient population in whom the ICD conferred a survival benefit or reduced death from arrhythmia. Of the randomized trials, the CABG-Patch was unique in that all patients received revascularization with CABG at the time of randomization. In CABG-Patch, 900 patients with an ejection fraction (EF) <0.36 and an abnormal signal-averaged ECG who were undergoing bypass surgery were randomized to receive an ICD using epicardial patches or not (12). After an average follow-up of 32 months, the hazard ratio (HR) for death from any cause was 1.07 (95% confidence interval [CI]: 0.81–1.42, $p = 0.64$). ICD implantation was associated with a higher rate of postoperative infections (ICD: 12.3% vs control: 5.9%; $p < 0.05$) and deep sternal wound infections (ICD: 2.7% vs 0.4%, $p < 0.05$). Patients were excluded if they had prior significant ventricular arrhythmias or poorly controlled diabetes. The Multicenter Unsustained Tachycardia Trial (MUSTT) enrolled 2202 patients with coronary artery disease, an EF ≤ 0.40, and nonsustained ventricular tachycardia (NSVT) ≥ 3 beats, of whom 704 had sustained ventricular tachycardia (VT) inducible by programmed electrical stimulation (10). The patients with inducible sustained VT were randomized to no antiarrhythmic therapy or antiarrhythmic therapy guided by electrophysiologic (EP) study. After a median follow-up of 39 months, the 5-year estimates for overall mortality were 42% and 48%, respectively (relative risk: 0.80; 95% CI: 0.64–1.01). Within the EP-guided therapy group, 161 patients received an ICD (after one or more failed antiarrhythmic drug trials), and in this

TABLE 1 Published Guideline Statements from Professional Societies That Make Recommendations on Implantation of ICDs Without Cardiac Resynchronization Capabilities

	"Secondary Prevention"	"Primary Prevention"
2006 ACC/AHA/ESC Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death	• ICD therapy is recommended for secondary prevention of SCD in patients who survived VF or hemodynamically unstable VT, or VT with syncope and who have an LVEF ≤40%, who are receiving chronic optimal medical therapy, and who have a reasonable expectation of survival with good functional status for more than 1 year. • An ICD should be implanted in patients with nonischemic DCM and significant LV dysfunction who have sustained VT or VF, are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with good functional status for more than 1 year. • Coronary revascularization is indicated to reduce the risk of SCD in patients with VF when direct, clear evidence of acute myocardial ischemia is documented to immediately precede the onset of VF. • If coronary revascularization cannot be carried out and there is evidence of prior MI and significant LV dysfunction, the primary therapy of patients resuscitated from VF should be the ICD in patients who are receiving chronic optimal medical therapy, and who have a reasonable expectation of survival with a good functional status for more than 1 year. • Patients presenting with sustained VT in whom low-level elevations in cardiac biomarkers of myocyte injury/necrosis are documented should be treated similarly to patients who have sustained ventricular tachycardia and in whom no biomarker rise is documented.	• ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF ≤30%–40%, are NYHA Class II or III receiving chronic optimal medical therapy, and have a reasonable expectation of survival with a good functional status for more than 1 year. • ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with nonischemic heart disease who have an LVEF ≤30%–35%, are NYHA Class II or III, are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with good functional status for more than 1 year.
2008 ACC/AHA/HRS Guidelines for Device-Based Therapy	• ICD therapy is indicated in patients who are survivors of cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes. • ICD therapy is indicated in patients with structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable. • ICD therapy is indicated in patients with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiologic study.	• ICD therapy is indicated in patients with LVEF <35% due to prior MI who are at least 40 days post-MI and are NYHA functional Class II or III. • ICD therapy is indicated in patients with nonischemic DCM who have an LVEF ≤35% and who are NYHA Class II or III. • ICD therapy is indicated in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF <30%, and are NYHA functional Class I. • ICD therapy is indicated in patients with nonsustained VT due to prior MI, LVEF <40%, and inducible sustained VT at electrophysiologic study.
2013 ACC/AHA Guideline for the Management of Heart Failure		• ICD therapy is recommended for primary prevention of SCD to reduce total mortality in selected patients with non-ischemic DCM or ischemic heart disease at least 40 days post-MI with LVEF of 35% or less and NYHA Class II or III symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for more than 1 year. • ICD therapy is recommended for primary prevention of SCD to reduce total mortality in selected patients at least 40 days post-MI with LVEF of 30% or less, NYHA Class I symptoms while receiving GDMT, who have a reasonable expectation of meaningful survival for more than 1 year.
2013 ACC/AHA Guideline for the Management of ST-Elevation Myocardial Infarction	• ICD therapy is indicated before discharge in patients who develop sustained VT/VF more than 48 hours after STEMI, provided the arrhythmia is not due to transient or reversible ischemia, reinfarction, or metabolic abnormalities.	

ACC = American College of Cardiology; AHA = American Heart Association; DCM = dilated cardiomyopathy; ESC = European Society of Cardiology; GDMT = guideline-directed medical therapy; HRS = Heart Rhythm Society; ICD = implantable cardioverter-defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; SCD = sudden cardiac death; STEMI = ST segment elevation myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

group, the adjusted relative risk of mortality was 0.40 (95% CI: 0.27-0.59). In the Multicenter Automatic Defibrillator Trial (MADIT), 196 patients with prior myocardial infarction, EF ≤0.35, and inducible nonsuppressible ventricular arrhythmias at electrophysiologic testing were randomized to receive an ICD or medical therapy alone (11). After an average follow-up of 27 months, the ICD was associated with a significant reduction in mortality (HR: 0.46; 95% CI: 0.26-0.82; p = 0.009). In the Multicenter Automatic Defibrillator Trial II (MADIT-II) 1232 patients with an EF ≤0.30 due to prior myocardial infarction were randomized to ICD therapy or medical therapy alone (2). During an average follow-up of 20 months, the ICD was associated with a significant reduction in mortality (HR: 0.69; 95% CI: 0.51-0.93; p = 0.016). Finally, the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) randomized 2521 patients with an ejection fraction ≤0.35 and Class II or III heart failure symptoms to

TABLE 2 Randomized Primary Prevention Trials of ICD therapy: Inclusion Criteria, Enrolled Patients, and Principal Findings

Study	Inclusion Criteria	Enrolled Patients	Findings
Ischemic Cardiomyopathy Multicenter Automatic Defibrillator Implantation Trial (MADIT) (11)	• Prior MI, LVEF ≤0.35; NSVT • Inducible nonsuppressible sustained VT/VF at EPS • >3 weeks post-MI • >2 months post-CABG • >3 months post-PTCA	• 196 patients enrolled, 95 in ICD arm • Mean age: 63 years • 92% male • Mean LVEF: 0.26 • 90 with prior CABG, 44 with prior PTCA, 53 with ≥2 prior MIs • 100% NSVT	• Reduced mortality with ICD (HR: 0.46; p = 0.009)
Coronary Artery Bypass Graft (CABG) Patch Trial (12)	• LVEF ≤0.35, abnormal SAECG, undergoing CABG	• 900 patients enrolled, 446 randomized to epicardial ICD implantation at time of CABG • Mean age: 64 years • 84% male • Mean LVEF: 0.27 • 100% CABG	• No difference in survival with ICD (HR: 1.07; 95% CI: 0.81–1.42; p = 0.64) • Arrhythmic mortality at 42 months: control 6.9%, ICD 4.0% (p = 0.057) - 45% reduction in arrhythmic death • 71% of deaths were nonarrhythmic: non-arrhythmic cardiac mortality at 42 months: control 12.4%, ICD 13.0% (p = 0.275)
Multicenter Unsustained Tachycardia Trial (MUSTT) (10)	• EF ≤0.40 • NSVT within the last 6 months • ≥4 days post-MI or revascularization	• 2202 patients enrolled, 704 patients with inducible VT, 161 received ICDs • Median age: 67 years • 90% male • Median EF: 0.30 • 56% prior CABG • 16% within 30 days of an MI • 100% NSVT • NYHA Class (I/II/II/IV): 37/39/24/0	• Risk of sudden death reduced in patients with ICDs (HR: 0.24; 95% CI: 0.13–0.45; p < 0.001)
Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) (2)	• >21 years old • EF ≤0.30 • >1 month after MI • >3 months after revascularization	• 1232 patients enrolled, 742 in ICD arm • Median age: 64 years • 84% male • EF: 0.23 • 57% prior CABG • NYHA Class (I/II/II/IV): 35/35/25/5	• After average f/u of 20 months, ICD group had lower mortality (HR: 0.69; 95% CI: 0.51–0.93; p = 0.016) • ICD associated with an absolute 5.6% decrease in mortality
Nonischemic Cardiomyopathy Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) (16)	• EF <36% due to NICM • NYHA Class I–III • NSVT or PVCs	• 458 patients enrolled, 229 received ICDs • Mean age: 58 years • 71% male • EF: 21% • NYHA Class (I/II/III): 22/57/21 • 216 patients (47%) with a recent diagnosis of NICM (≤9 months)	• After mean f/u of 29 months, trend for reduced mortality in the ICD group (HR: 0.65; 95% CI: 0.40–1.06; p = 0.08) and a significant decrease in sudden death due to arrhythmias (HR: 0.20; 95% CI: 0.06–0.71; p = 0.006) • Subanalysis showed similar ICD benefit in patients with recently identified NICM (<9 months) compared with remote diagnosis
Both Ischemic and Nonischemic Cardiomyopathy Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) (1)	• 18 years old • EF <35% • NYHA Class II or III	• 2521 patients enrolled, 829 received ICDs • Median age: 60 years • 76% male • EF: 0.25 • 33 patients within 30 days of an MI • 23% NSVT • NYHA Class (I/II/II/IV): 0/70/30/0	• After median f/u of 46 months, ICD group had lower mortality (HR: 0.77; 97.5% CI: 0.62–0.96; p = 0.007) compared with placebo or amiodarone groups • ICD associated with an absolute 7.2% decrease in mortality

Acute Coronary Artery Disease Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) (14)	• 18–80 years old
	• MI past 6–40 days
	• EF <0.35
	• Abnormal HRV
		• 674 patients enrolled, 332 received ICDs
		• Average age: 61 years
		• 76% male
		• EF: 0.28
		• Index MI:
		  • 72% Anterior
		  • 72% new Q wave
		  • Peak CK: 2300 U/L
		  • Reperfusion: 63%
		  • 26% PCI
		  • 27% thrombolysis
		  • 10% both
			• After mean f/u of 30 months, no difference in mortality between ICD and no ICD groups (HR: 1.08; 95% CI: 0.76–1.55; p = 0.66)
			• ICD group had a significant decrease in risk of death due to arrhythmia (HR: 0.42; 95% CI: 0.22–0.83; p = 0.009) but a significant increase in risk of nonarrhythmic death (HR: 1.75; 95% CI: 1.11–2.76; p = 0.02)

Immediate Risk Stratification Improves Survival Study (IRIS) (15)	• MI in the past 5–31 days and *either*:
	• EF ≤40% and initial HR >90 bpm
	• NSVT >150 bpm
		• 898 enrolled, 445 received ICDs
		• Average age: 63 years
		• 77% male
		• EF: 0.35
		• Index MI:
		  • 64% anterior
		  • 77% STEMI
		  • Reperfusion: 77%
		  • 72% PCI
		  • 16% thrombolysis (+/- PCI)
			• After mean f/u of 37 months, no difference in mortality between the ICD and no ICD groups (HR: 1.04; 95% CI: 0.81–1.35; p = 0.78)
			• ICD group had a significant decrease in sudden cardiac death (HR: 0.55; 95% CI: 0.31–1.00; p = 0.049) but a significant increase in risk of nonsudden cardiac death (HR: 1.92; 95% CI: 1.29–2.84; p = 0.001)

MI = myocardial infarction; LVEF = left ventricular ejection fraction; VT = ventricular tachycardia; VF = ventricular fibrillation; NSVT = nonsustained ventricular tachycardia; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; ICD = implantable cardioverter defibrillator; NYHA = New York Heart Association; HR = hazard ratio; NICM = nonischemic cardiomyopathy; PVCs = premature ventricular contractions; HRV = heart rate variability; STEMI = ST segment elevation myocardial infarction.

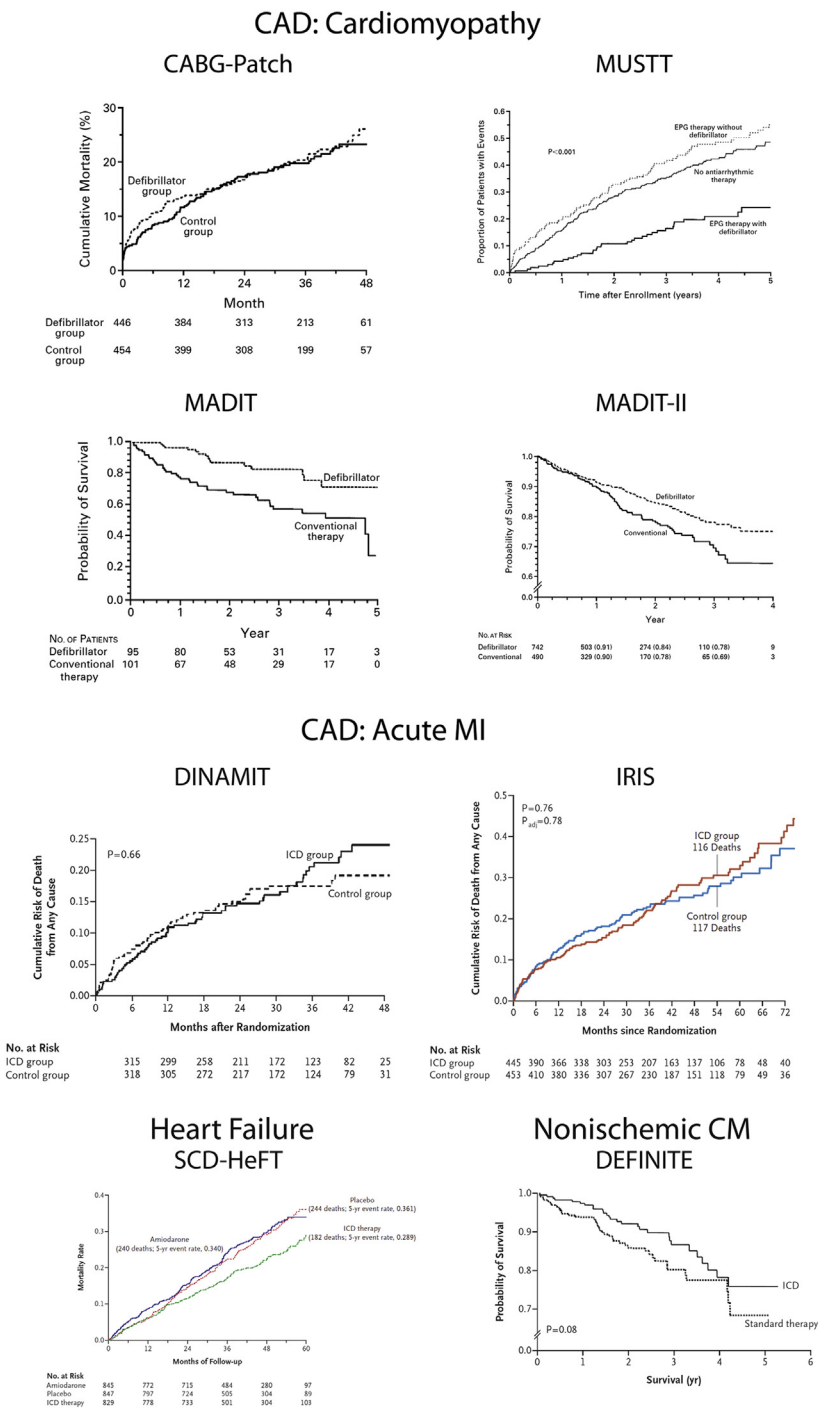

FIGURE 1 Survival Curves for the ICD-Only Primary Prevention Trials in Patients With Cardiomyopathy (CM) Due to Coronary Artery Disease (CAD) or Acute Myocardial Infarction (MI), Heart Failure, or Nonischemic CM

All curves represent mortality/survival. MADIT = Multicenter Automatic Defibrillator Trial; MUSTT = Multicenter Unsustained Tachycardia Trial; CABG-Patch = Coronary Artery Bypass Graft-Patch; DINAMIT = Defibrillator in Acute Myocardial Infarction Trial; IRIS = Immediate Risk Stratification Improves Survival Study; SCD-HeFT = Sudden Cardiac Death in Heart Failure Trial; DEFINITE = Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation Trial. (With Permission New England Journal of Medicine.)

ICD therapy, placebo, or amiodarone. In SCD-HeFT slightly more than 50% of patients had cardiac dysfunction and heart failure due to coronary artery disease. After a median follow-up of 45 months, ICD therapy was associated with a significant reduction in mortality (HR: 0.77; 97.5% CI: 0.62–0.96; p = 0.007) (1).

It is instructive to examine the clinical characteristics of patients who were actually enrolled in the trials (**Table 2**) (1,2,10–12). The median age of enrolled patients was 63–67 years, and patients >75 years accounted for 554 (11%) of the patients enrolled in MUSTT, MADIT-I, MADIT-II, and SCD-HeFT (13). The trials predominantly studied men, with women accounting for only 8%–24% of enrollees. Ethnic background was identified in the MUSTT and SCD-HeFT trials. Nonwhite patients accounted for 9% of patients in MUSTT and 24% of patients in SCD-HeFT. The baseline cardiovascular characteristics varied between the trials. Although EF was similar for all five trials, ranging from 0.23–0.30, 80% of patients in MUSTT had Class I or II heart failure symptoms, 70% of patients in MADIT II had Class I or II heart failure symptoms, and 67% of patients in MADIT and 100% of patients in SCD-HeFT had Class II or III heart failure symptoms. Prior revascularization with CABG also varied among the three studies, at approximately 50% of patients with ischemic cardiomyopathy in SCD-HeFT, 45% in MADIT, 56% in MUSTT, 57% in MADIT-II, and of course 100% in CABG-Patch. NSVT was part of the inclusion criteria for MADIT and MUSTT and thus was present in all patients but was present in only 23% of patients in SCD-HeFT. The incidence of NSVT was not provided in initial or subsequent reports on the CABG-Patch or MADIT-II trials.

Two trials have evaluated the use of ICDs in patients in the acute period after MI (14,15). In the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), 674 patients were randomized between 6 to 40 days after an MI to receive an ICD or no ICD therapy (14). Additional inclusion criteria included a left ventricular ejection fraction (LVEF) ≤0.35 and impaired cardiac autonomic function. After a mean follow-up of 30 months, there was no mortality benefit associated with the ICD implant (HR: 1.08; 95% CI: 0.76–1.55; p = 0.66). In the Immediate Risk-Stratification Improves Survival (IRIS) trial, 898 patients were randomized between 5 to 31 days after an MI to receive an ICD or no ICD therapy (15). Unlike DINAMIT, patients could be enrolled in IRIS under two clinical scenarios, either an LVEF ≤0.40 associated with an initial sinus rate >90 bpm, or NSVT (>3 beats at a rate >150 bpm) identified by 24-hour ambulatory ECG. After a mean follow-up of 37 months, ICD therapy was not associated with a significant reduction in mortality (HR: 1.04; 95% CI: 0.81–1.35; p = 0.78). Similar to the primary prevention trials discussed previously, both studies predominantly enrolled men (76%–77%) who were in their early 60s (average age 61–63 years). As expected, the average LVEF was higher in IRIS (0.35) when compared with DINAMIT (0.28) because 23% of patients were enrolled in IRIS based on the presence of NSVT. In both studies, anterior wall MIs accounted for two-thirds of the index MIs. Reperfusion therapy in DINAMIT was performed in approximately 60% of patients, evenly split between thrombolysis and percutaneous coronary intervention (PCI). Reperfusion therapy was attempted in 77% of patients in IRIS, with three-fourths of these patients receiving PCI.

Two large studies on ICD therapy in patients with nonischemic cardiomyopathy have been completed (1,16). In SCD-HeFT, 1211 patients (slightly less than 50% of the total group) had heart failure due to nonischemic cardiomyopathy (1). In a prespecified analysis of this patient group, ICD therapy conferred a trend toward a survival advantage (HR: 0.73; 97.5% CI: 0.50–1.07; p = 0.06). The apparent decrease in the magnitude of benefit conferred by the ICD is in part explained by the lower event rate observed in patients with nonischemic cardiomyopathy when compared with patients with ischemic cardiomyopathy (5-year event rate with ICD therapy: ischemic 0.359 vs nonischemic 0.214). The Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial evaluated only patients with nonischemic cardiomyopathy (16). A total of 458 patients with nonischemic cardiomyopathy, LVEF <0.36, and frequent premature ventricular contractions or NSVT were randomized to ICD therapy or no ICD therapy. After a mean follow-up of 29 months, there was a trend toward improved survival with ICD (HR: 0.64; 95% CI: 0.40–1.06; p = 0.08) and a significant reduction in deaths due to arrhythmia with ICD therapy (HR: 0.20; 95% CI: 0.06–0.71; p = 0.006). The patients enrolled in DEFINITE were younger (average age 58 years) and had a lower ejection fraction (0.21) than the patients enrolled in the trials that evaluated the benefits of ICD therapy in patients with coronary artery disease.

4. ICD IMPLANTATION IN THE CONTEXT OF AN ABNORMAL TROPONIN THAT IS NOT DUE TO A MYOCARDIAL INFARCTION

***Patient Population #1**: Patients with an abnormal troponin level (or other biomarker for myocardial infarction) who do not fulfill criteria for MI, and previously satisfied primary prevention or secondary prevention criteria for ICD implantation.*

Recommendation:

- In patients with abnormal cardiac biomarkers that are not thought to be due to an MI and who otherwise would be candidates for implantation on the basis of primary prevention or secondary prevention criteria, implantation of an ICD *is recommended*.

Discussion: A diagnosis of "acute MI" is defined by a unique and specific set of clinical and laboratory criteria. The detection of elevated cardiac biomarkers alone is not sufficient to satisfy this definition.

The diagnostic criteria for acute MI, established by the joint ESC/ACC/AHA/WHF Task Force, are the following (17):

An appropriate rise and/or fall in cardiac biomarkers with at least one value above the 99th percentile upper reference level, together with evidence of myocardial ischemia and with at least ONE of the following:

- Electrocardiographic evidence of new ischemia (ST segment shift or development of left bundle branch block [LBBB])
- Evolution of pathologic Q waves on the electrocardiogram
- Imaging evidence of new regional wall motion abnormality or new loss of viable myocardium
- Ischemic symptoms

Cardiac biomarkers (MB fraction of creatine kinase [CKMB] or troponin) can rise in clinical circumstances other than acute myocardial infarction, such as kidney disease, acute pulmonary embolus, heart failure, myocarditis, chest trauma, or tachyarrhythmia. These biomarkers have been reviewed in the ACC 2012 expert consensus document on practical clinical considerations in the interpretation of troponin elevations (**Figure 2**) (18). The diagnosis of MI implies myocyte necrosis due to an ischemic insult and should be reserved for patients who satisfy the above diagnostic criteria. Patients who do not meet these criteria need to be evaluated quite differently in terms of suitability for ICD therapy. The requirement to delay ICD implantation for 40 days after presentation is

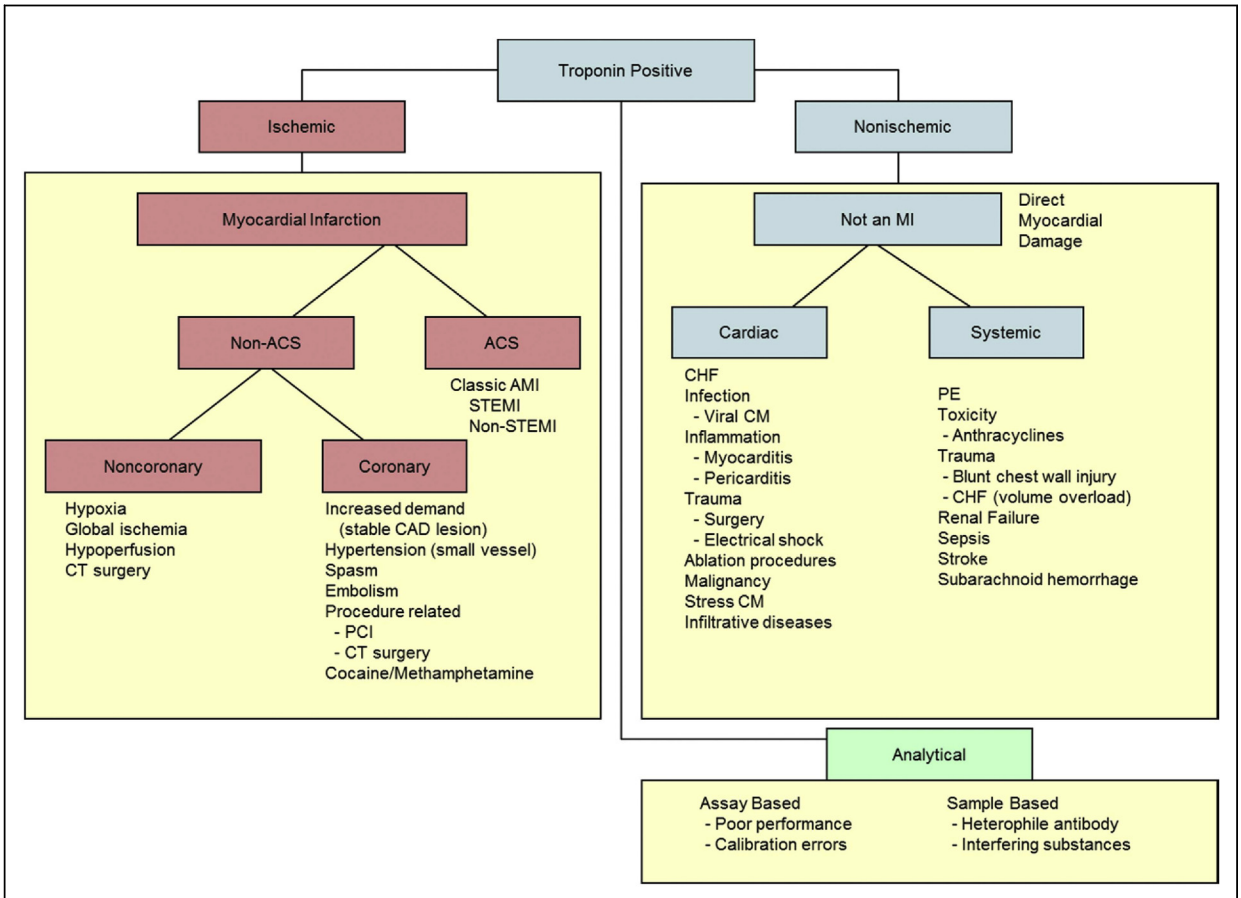

FIGURE 2 Ischemic and Nonischemic Causes of Abnormal Troponin

ACS = acute coronary syndrome; AMI = acute myocardial infarction; CAD = coronary artery disease; CHF = congestive heart failure; CM = cardiomyopathy; CT = cardiothoracic; MI = myocardial infarction; PCI = percutaneous coronary intervention; PE = pulmonary embolism; STEMI = ST segment elevation myocardial infarction. (From Newby et al. [17]. Used with permission from the American College of Cardiology.)

not applicable if a clear diagnosis of acute MI is not established. This mandatory waiting period should not be imposed on patients who would otherwise qualify for an ICD for either primary or secondary prevention.

5. ICD IMPLANTATION WITHIN 40 DAYS OF A MYOCARDIAL INFARCTION

In the great majority of situations, ICD implantation should be performed at least 40 days after an MI. During the acute phase of MI, it is often unclear how much recovery of cardiac function will occur following hospital discharge, and in some cases, the clinical condition is so severe that ICD implantation would be of little value. The 2008 Device-Based Guidelines emphasize this point, largely based on the negative results of DINAMIT and later confirmed by the publication of IRIS (5). Despite the results of these clinical trials, the writing group identified several scenarios in which clinicians may consider implanting an ICD within 40 days of an MI (Figure 3). For each of these scenarios we will review the data pertaining to this topic and provide Consensus Recommendations for ICD implantation.

***Patient Population #2**: Patients within 40 days of acute MI who have known left ventricular dysfunction and who have previously satisfied criteria for implantation of a primary prevention ICD.*

Recommendation:

- Implantation of an ICD within the first 40 days following acute MI in patients with preexisting systolic ventricular dysfunction (who would have qualified for a primary prevention ICD) *is not recommended.*

Discussion: Patients who present an acute coronary syndrome can have preexisting left ventricular dysfunction due to prior ischemic events or a cardiomyopathic process. The 6-month period immediately following an acute MI confers a high risk of sudden death (19,20). In

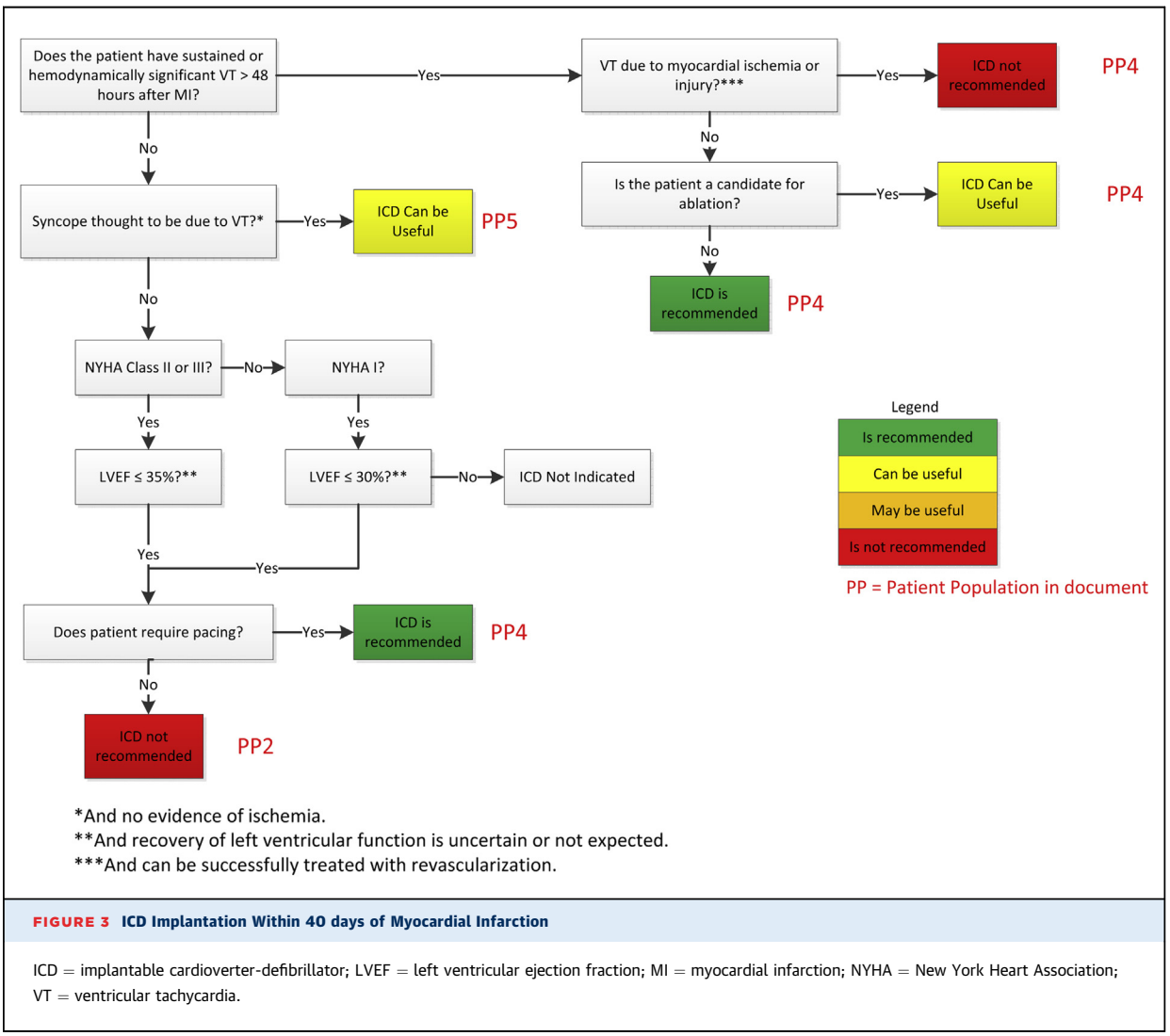

FIGURE 3 ICD Implantation Within 40 days of Myocardial Infarction

ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; VT = ventricular tachycardia.

the Valsartan in Acute Myocardial Infarction Trial (VALIANT), the risk of sudden death was highest in the first 30 days after an MI, at 1.4% per month, and decreased to 0.14% per month after 2 years (20).

A survival advantage was clearly demonstrated in the MADIT-II trial for patients receiving ICD therapy after MI (2). The study population included patients with an MI >1 month from study entry and an LVEF ≤0.30. There was no requirement for electrophysiologic testing. However, as illustrated by the survival curves in **Figure 1**, the benefit did not become evident until approximately 9 months after device implantation. Similarly, separation of the survival curves in SCD-HeFT was also observed 12–15 months after device implantation (**Figure 1**) (1).

Given the high risk of sudden death in the early post-MI period and the benefits of ICD therapy in patients with cardiac dysfunction due to MI, it would seem intuitive that ICD implantation early after MI would be beneficial. However, two separate randomized trials have failed to show an advantage to ICD implantation within 30–40 days after MI (DINAMIT, IRIS) (14,15). The DINAMIT trial failed to show early survival benefits in patients who underwent ICD implantation within 6–40 days of an acute infarct. There was a highly statistically significant reduction in the incidence of arrhythmic death (95% CI: 0.22–0.83; p = 0.009) for patients receiving an ICD. This was balanced, however, by an increased incidence of nonarrhythmic death; thus, overall survival was not improved (14). Patients in IRIS were enrolled within 1 month of the index infarction, and once again there was a 45% lower risk of sudden death in the ICD group. However, this lower risk was offset by a significantly increased risk of nonarrhythmic death in the control patients (p = 0.001) (15). Although DINAMIT and IRIS did not specifically study the patient population in question (implantation of an ICD following an acute MI with preexisting systolic dysfunction), neither provided evidence of a survival advantage conferred by early implantation of an ICD.

Subsequent analysis of VALIANT and DINAMIT has provided a likely pathophysiologic mechanism for the absence of benefit of ICD implantation in the early period after myocardial infarction (21,22). In DINAMIT, only 50% of the sudden deaths were attributable to arrhythmia, whereas mechanical causes of SCD (e.g., LV rupture, acute mitral regurgitation) were observed in the other half of patients (21). Similarly in VALIANT, investigators evaluated the available autopsy records in patients who experienced sudden death (22). In the first month after MI, 80% of sudden cardiac deaths appeared to be due to recurrent MI or rupture, and presumed arrhythmia death only accounted for the remaining 20% of sudden cardiac deaths. By 1 year, the proportions of sudden deaths due to nonarrhythmia vs arrhythmia causes were equal, and over time there appeared to be a very gradual increase in the proportion of sudden deaths due to arrhythmia (approximately 60% at 30 months). Therefore, it would not be anticipated that early implantation of an ICD in this patient population would significantly impact these deaths. It can also be argued that early ICD implantation in these patients can actually "cause harm" and negatively impact survival. Ventricular remodeling following an acute MI can produce new substrates for ventricular arrhythmia. Patients randomized to ICD therapy in the DINAMIT study who died were those who received shocks for ventricular arrhythmias. These patients also had more recurrent myocardial ischemia and more heart failure events (21). Supporting this hypothesis is a retrospective subanalysis of patients who received ICDs and subsequent shocks in MADIT-II (23). Patients randomized to ICD therapy had a significant increase in the risk of first heart failure events (HR: 1.39; p = 0.02) that was more pronounced in those patients who received shocks (HR: 1.9; p = 0.01). The study authors postulated that defibrillator shocks can result in injury to the myocardium, and that ventricular function can be further impaired as a consequence of backup ventricular pacing. Finally, a review of a large single-center database of 16,793 patients who were referred to the cardiac catheterization laboratory for acute management of MI found a 90-day cardiovascular mortality rate of 9%, with 75% of the deaths judged to be coronary artery disease-related nonsudden death, 9% coronary artery disease-related sudden death, and 4% due to sudden death not related to coronary artery disease (24).

Aggressive therapy to reduce the risk of sudden cardiac death in the early period after MI directed toward revascularization and improvement in left ventricular function and clinical heart failure can be a more prudent and effective strategy as compared with early ICD implantation. Although the ACC/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 Appropriate Use Criteria for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy have provided "appropriate" scores (8 and 9) for ICD implantation in this patient population, the consensus of this group is that implantation of an ICD is not recommended within the first 40 days after the MI unless other potential reasons for an ICD implant are present (patient populations 3-6) (9).

***Patient Population #3**: Patients within 40 days of an acute MI who also have an indication for permanent pacemaker implantation.*

Recommendation:

- In patients who, within 40 days of an MI, require nonelective permanent pacing, who also would meet primary prevention criteria for implantation of an ICD, and recovery of left ventricular function is uncertain or not expected, implantation of an ICD with appropriately selected pacing capabilities *is recommended*.

Discussion: Guidelines have been established that clearly direct the clinician to identify the rhythm abnormalities that require pacing support in patients following MI (5). In the presence of normal or mildly reduced left ventricular function there would be no rationale for expanding the guidelines to include ICD therapy. In the circumstance in which the patient's LVEF is ≤0.35 (or LVEF ≤0.40 with ambient NSVT and positive EP study), one needs to consider whether using an ICD platform when implanting the permanent pacemaker (PPM) is reasonable. This reflects the fact that implantation of a pacemaker or ICD is associated with some risk, especially infection. If the likelihood that a patient requiring PPM implantation early post-MI will ultimately require a second procedure to extract the PPM and leads and replace it with an ICD system 40 days later, it would seem inappropriate not to implant an ICD rather than a PPM. Therefore, if a patient requires urgent nonelective implantation of a PPM within 40 days of an MI, and recovery of ventricular systolic function is uncertain or not anticipated, implantation of an ICD platform with appropriately selected pacing capability is appropriate. This approach not only avoids subjecting the patient to a second procedure and its attendant risks, it also lowers total cost. The choice of a single, dual, or biventricular system should be based upon the clinical setting, current guidelines, and consensus documents that address this decision under general conditions. The 2013 AUC document for ICDs also gives an "appropriate" score in this situation (9).

In contrast to the scenario outlined above, if recovery of ventricular contractility can be anticipated with a high degree of certainty, then it would be appropriate to implant a PPM. Similarly, if pacemaker implantation for heart rate support can be delayed, it is prudent to wait until recovery of left ventricular function can be assessed.

Patient Population #4: *Patients within 40 days of an MI who subsequently present sustained or hemodynamically significant ventricular tachyarrhythmias.*

Recommendations:

- In patients who, within 40 days of an MI, develop sustained (or hemodynamically significant) ventricular tachyarrhythmias >48 hours after an MI and in the absence of ongoing ischemia, implantation of an ICD *is recommended.*
- In patients who, within 40 days of an MI, develop sustained (or hemodynamically significant) VT >48 hours after an MI that can be treated by ablation, implantation of an ICD *can be useful.*
- In patients who, within 40 days of an MI, develop sustained (or hemodynamically significant) ventricular tachyarrhythmias where there is clear evidence of an ischemic etiology with coronary anatomy amenable to revascularization (and appropriately treated), implantation of an ICD *is not recommended*.

Discussion: The risk of ventricular tachyarrhythmias in patients with acute MI is highest at the time of presentation and declines over the hours and days that follow (19).

Several studies have evaluated the frequency and prognosis associated with sustained ventricular tachyarrhythmias in the setting of an ST segment elevation MI (STEMI) (25–28). In the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarcto Miocardico (GISSI-2) database, the incidence of early-onset (≤4 hours) and later (>4 to 48 hours) sustained VT or ventricular fibrillation (VF) was 3.1% and 0.6%, respectively (25). Patients who developed early VF had a more complicated course than matched controls, and development of VF, regardless of timing, was an independent predictor of in-hospital mortality. However, the postdischarge to 6-month death rates were similar for those patients who developed VF and those patients who did not. In an analysis of 40,895 patients enrolled in the Global Use of Streptokinase tPA for occluded coronary arteries (GUSTO-1) trial, 4188 (10.2%) had significant sustained ventricular tachyarrhythmias split approximately evenly between VF and VT (26). Patients with ventricular tachyarrhythmias had higher in-hospital mortality rates (VT: 19%; VF: 24%; both: 44%) and 30-day mortality rates (VT: 18%; VF: 24%; both: 45%) than patients without ventricular tachyarrhythmias (in-hospital mortality: 4.2%; 30-day mortality: 4.6%). Among patients who survived hospitalization, no significant difference was found in the 30-day mortality between the ventricular tachyarrhythmia and no ventricular arrhythmia groups. However, in patients who survived at 30 days, 1-year mortality rates were higher in patients with VT (7.2%) or both VT and VF (7.1%) when compared with the patients with either VF (2.9%) or neither type of arrhythmia (2.7%). In general, developing sustained ventricular tachyarrhythmias >2 days after hospital admission was associated with a poorer prognosis (1-year mortality in 30-day survivors: VT: 24.7%, VF: 6.1%, both: 4.7%). More recently, in an analysis of the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-MI) trial, 5.7% of patients presenting STEMI had sustained ventricular tachyarrhythmias, with 90% of ventricular tachyarrhythmias occurring within the first 48 hours (27). In a multivariate analysis, patients with early ventricular tachyarrhythmias had a higher heart rate, Killip class, and total ST segment deviation. At 90 days, mortality was higher for patients with ventricular tachyarrhythmias compared with those patients without ventricular tachyarrhythmias (23.6% vs 3.6%, adjusted HR: 3.63; 95% CI: 2.59–5.09). Of the patients who developed sustained ventricular tachyarrhythmias, ventricular

tachyarrhythmias occurred before the end of the cardiac catheterization in two-thirds of the patients, while the remaining third developed ventricular tachyarrhythmias after leaving the cardiac catheterization laboratory. The 90-day mortality rate was significantly higher in those patients who developed ventricular tachyarrhythmias after leaving the cardiac catheterization laboratory (33%) compared with those patients who developed ventricular tachyarrhythmias before or during cardiac catheterization (17%). Finally, in an analysis of the pooled data from the four Primary Angioplasty in Myocardial Infarction (PAMI) trials, approximately 4% of patients developed sustained ventricular tachyarrhythmias during PCI (28). In-hospital and 4-year mortality were similar between patients who developed sustained ventricular tachyarrhythmias during PCI and those patients who did not.

Increased mortality is also observed in patients who develop ventricular tachyarrhythmias in the setting of a non-ST segment elevation MI (NSTEMI). The PURSUIT trial evaluated the impact of a glycoprotein IIb/IIa inhibitor on mortality or myocardial infarction patients with NSTEMI (29). In this population, the onset of either VT or VF was associated with an increase in 30-day mortality (HR: 23.2). Similarly, in an analysis of the Early Glycoprotein IIb/IIIa Inhibition in NSTE ACS (EARLY ACS) trial, sustained ventricular tachyarrhythmias were observed in 1.5% of patients, with 0.6% occurring ≤48 hours after enrollment (30). The risk of death at 1 year relative to patients without ventricular tachyarrhythmias was dramatically greater in those patients with ventricular tachyarrhythmias >48 hours (HR: 20.7; 95% CI: 15.39-27.85) when compared with patients with ventricular tachyarrhythmias ≤48 hours (HR: 7.45; 95% CI: 4.60-12.08).

The development of ventricular tachyarrhythmias after the acute phase depends in large part on the extent of left ventricular dysfunction. Patients enrolled in the VALIANT trial with an LVEF ≤0.30 demonstrated the highest incidence of early cardiac arrest or sudden death (20). In a subsequent analysis of the 164 patients who had successful resuscitation after sudden death in VALIANT, 75 had cardiac arrest within the first 40 days after myocardial infarction (31). Investigators felt that ICD implantation would have been beneficial in 16 of these patients, with a median time of 11 days between cardiac arrest and ICD implant. ICD implantation was associated with a nonsignificant decrease in mortality (HR: 0.44; 95% CI: 0.10-2.01; p = 0.29), although the sample size was small and would have only identified a very large benefit in terms of mortality. Although the AVID trial allowed enrollment of patients within 5 days of a myocardial infarction, and 67% of patients had a history of myocardial infarction, it is not clear how many patients were enrolled within 40 days of a myocardial infarction. In addition, it is notable that more than 60% of patients had no angina prior to the event, and patients who were thought to have a transient or correctable cause for ventricular tachyarrhythmias were enrolled in the registry rather than the main trial (3).

These data indicate that patients with ventricular tachyarrhythmias following MI are at risk of catastrophic events such as cardiac arrest or sudden death, and that the risk is highest within the first 30-60 days following MI. This is particularly true for patients with left ventricular systolic dysfunction. Implantation of an ICD in this population is reasonable in selected patients in the absence of opportunities for revascularization. When there is evidence of reversible ischemia that is responsible for the ventricular tachyarrhythmia, revascularization options need to be implemented as an initial strategy before committing the patient to ICD therapy. In particular, VF that occurs within the first several hours after the onset of symptoms of an acute MI has not been associated with an increased risk of late sudden cardiac death. Finally, some ventricular tachyarrhythmias can be effectively treated with catheter ablation (32). In patients with idiopathic VT (e.g., right ventricular outflow tract tachycardia), catheter ablation would effectively eliminate the arrhythmia and ICD therapy is not required. However, even patients with VT easily amenable to ablation (e.g., bundle branch reentry) can remain at significant risk of other ventricular tachyarrhythmias due to the presence of structural heart disease, and the clinician must decide whether an ICD is appropriate on an individual basis.

Patient Population #5*: Patients who, within 40 days of an MI (but >48 hours), present with syncope likely due to ventricular tachyarrhythmia, and in whom there is no evidence of ongoing ischemia.*

Recommendation:

- In patients who, within 40 days of an MI, present with syncope that is thought to be due to ventricular tachyarrhythmia (by clinical history, documented NSVT, or electrophysiologic study), implantation of an ICD *can be useful.*

Discussion: Patients with syncope in the setting of structural heart disease have an increased incidence of sudden death and overall mortality (6,8,9). The ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy specify a Class I indication for ICD implant for "patients with syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study" (5). This recommendation is based primarily on the Canadian Implantable Defibrillator Study (CIDS), which specifically included unmonitored syncope patients either who were later identified as having spontaneous VT of at least 10

seconds or who were inducible for sustained monomorphic VT (33). It is important to note that these inclusion criteria were applicable for only 87 of the 659 patients enrolled in CIDS, and the point estimate was approximately 0.95 with very wide confidence intervals. The 2006 Guidelines on Ventricular Arrhythmias provide a Class I recommendation for an EP study for the diagnostic evaluation of patients with a remote MI with symptoms suggestive of ventricular tachyarrhythmias such as syncope (6). Performance of an EP study appears to be safe after myocardial infarction, and inducible monomorphic VT does appear to identify a group with higher mortality (34). No study has specifically evaluated the use of an EP study in patients with syncope in the first 40 days after a myocardial infarction.

Based on our literature search, we have identified no studies that have specifically addressed whether ICD implantation is beneficial in the setting of syncope thought to be due to a ventricular tachyarrhythmia in the first 40 days after MI. However, the consensus of the writing group is that syncope in the setting of a recent MI is a potentially serious issue, and ICD implantation can be useful if syncope is thought to be due to a ventricular tachyarrhythmia (by clinical history, documented NSVT, or EP study), regardless of timing in relationship to an MI (either $<$40 days or $\geq$40 days after MI).

Patient Population #6: *Patients within 40 days of an MI who have a previously implanted ICD that requires elective replacement for battery depletion.*

Recommendation:

- In patients within 40 days of an MI and who have an ICD that requires elective replacement due to battery depletion, after careful assessment of comorbidities and the current clinical situation, replacement of the ICD generator *is recommended.*

Discussion: An ICD approaching the end of its service is typically replaced. The absence of ICD shock or a requirement for antitachycardia therapies during the first battery service period does not indicate that an ICD is no longer required. There is evidence that up to 14% of patients who receive an ICD for primary prevention and whose first battery period is uneventful will require device therapy in the following 2.5 years (35).

In patients who undergo ICD implantation for primary prevention, the indication for device therapy persists following MI, particularly if there has been further deterioration of left ventricular function. Similarly, patients who receive device therapy for secondary prevention should be eligible for generator replacement following MI. In addition, the original indications for ICD implantation should be reviewed. The clinician needs to apply clinical judgment to determine whether there are new comorbidities that impact life expectancy in making this decision.

Patient Population #7: *Patients with significant left ventricular dysfunction within 40 days following an acute MI who are also listed for heart transplantation or who undergo implantation of a left ventricular assist device.*

Recommendation:

- ICD implantation in patients within 40 days of an MI who have been listed for heart transplant or implanted with a left ventricular assist device is *not recommended.*

Discussion: There is very little scientific evidence available to address this issue. Patients presenting refractory heart failure and/or hemodynamic instability typically require mechanical support such as a ventricular assist device (VAD) or extracorporeal membrane oxygenation (ECMO). Implantation of an ICD in this scenario is rarely a consideration because there is no clear evidence of benefit.

There are a few studies that have evaluated the benefit of ICD therapy following resuscitated sudden death or as primary prevention in patients waiting for transplant (36–41). However, most of these studies are fairly small and nonrandomized. There are certainly no data to support ICD therapy in patients within 40 days of an MI who are waiting for cardiac transplant. Large clinical trials such as SCD-HeFT and MADIT-II did not include patients with Class IV heart failure (1,2). In addition, the survival benefit with ICD implantation was not observed until 1 year after enrollment. Given the associated risk of nonsudden cardiac death and the higher likelihood of sudden death not due to ventricular arrhythmias, ICD implantation in patients within the first 40 days after MI who are waiting for transplant is not supported by current evidence. The wearable cardioverter-defibrillator (WCD) may be an option as a "bridge to ICD" for selected patients at high risk of sudden cardiac death due to ventricular arrhythmias, although the data are scant (42).

6. ICD IMPLANTATION WITHIN 90 DAYS OF REVASCULARIZATION

Patient Population #8A: *Patients within 90 days of revascularization who have known left ventricular dysfunction and who have previously satisfied criteria for implantation of a primary prevention ICD.*

Recommendation:

- In patients who are within 90 days of revascularization and who previously qualified for the implantation of an ICD for primary prevention of sudden cardiac death, and who have undergone revascularization that is

unlikely to result in an improvement in LVEF >0.35, and who are not within 40 days after an acute MI, implantation of an ICD *can be useful*.

Discussion: An analysis of the survival benefit with an ICD in the first 90 days after revascularization is lacking from the large, randomized, primary prevention trials. In their study designs, MADIT excluded subjects within 2 months after CABG and 3 months after PTCA, and MADIT-II excluded subjects within 3 months after revascularization (2,11). Conversely, early revascularization was permitted in MUSTT, which enrolled subjects at least 4 days after revascularization, and SCD-HEFT made no specific exclusion with respect to the timing of revascularization (1,10). However, in SCD-HEFT, the median time from CABG to enrollment was 3.1 years, and from PCI to enrollment was 2.3 years. Therefore, the published device-based therapy guidelines do not specifically address ICD implantation within 90 days of coronary revascularization for patients who otherwise meet ICD implant criteria for primary prevention of sudden cardiac death (5).

Revascularization has important time-dependent benefits. In the untreated arm of MUSTT, 228 subjects had postoperative NSVT (within 30 days after CABG) and 1302 had nonpostoperative NSVT (in patients who had no prior CABG or who were at least 30 days after CABG) (43). The postoperative NSVT group had slower VT, higher LVEF (0.30 vs 0.28, p = 0.002), shorter time from most recent MI, less heart failure, and higher use of beta-blockers and aspirin, but more multivessel coronary artery disease, lower use of Angiotensin Converting Enzyme inhibitors (ACE), diuretics, calcium channel blockers, and nitrates. This group had a lower inducibility rate for sustained monomorphic VT (27% vs 33%) and lower rates of 2- and 5-year arrhythmic events (6% vs 15% at 2 years, 16% vs 29% at 5 years) and overall mortality (15% vs 24% at 2 years, 36% vs 47% at 5 years). Substudies of the primary prevention trials (MADIT-II, MADIT-CRT, and SCD-HEFT) show that an ICD has an increasing survival benefit as time from revascularization increases (44–46). In a MADIT-II substudy of 951 patients with prior coronary revascularization, an ICD was of benefit only in patients enrolled at least 6 months after revascularization (45). In another MADIT-II substudy of 563 patients who received an ICD and underwent coronary revascularization, for every year that elapsed from coronary revascularization there was an associated 6% increase in 8-year mortality and a 5% increase in appropriate ICD therapy (46). In a substudy of MADIT-CRT, the rate of VT/VF or death was lower early (<1.5 years) compared with later after revascularization (44). Finally, a SCD-HeFT substudy of ischemic heart disease patients not randomized to amiodarone showed that prior PCI was associated with reduced mortality risk and CABG was associated with reduced sudden death risk, with a trend for improved survival if CABG occurred more than 2 years prior to enrollment (47). A retrospective observational study of patients with ischemic cardiomyopathy who underwent CABG also showed an improved survival for patients who subsequently were implanted with an ICD than those who did not receive an ICD, with a mean time to implant in ICD patients of 2 years (48). However, a limitation of these studies was that they analyzed patients several months to years from revascularization, and not within 90 days from revascularization. An exception was the CABG-Patch trial that randomized patients to ICD therapy using epicardial leads or no ICD at the time of CABG. There was no difference in survival with an ICD (HR 1.07; 95% CI: 0.81–1.42; p = 0.64), although there was a 45% borderline significant reduction in arrhythmic death (p = 0.0570) (12,49). In a subanalysis of CABG-Patch, patients with poorer left ventricular function as assessed by a wall motion score ≤16% (using centerline chord motion analysis from a ventriculogram) showed improved survival when treated with an ICD (ICD 4 year-survival: 0.72 vs no ICD 4-year survival: 0.56; p = 0.046) (50). In this analysis, although patients had poorer left ventricular function as assessed by a wall motion score, LVEF was not significantly different by left ventricular angiography emphasizing the difficulties in assessing left ventricular function.

The risk of sudden death early after revascularization is unclear. As mentioned above, in a substudy of MUSTT, patients enrolled within 30 days of CABG had significantly lower rates of arrhythmic events and total mortality, despite other high-risk characteristics, than patients not enrolled within 30 days after CABG. In a substudy of the Beta-Blocker Evaluation of Survival Trial (BEST), patients with ischemic heart failure (LVEF ≤35%) and prior CABG also had lower all-cause mortality, but sudden cardiac death was unchanged when compared with propensity-matched patients without CABG (51). Furthermore, patients with significantly reduced left ventricular function display poor survival early (within the first few months) after coronary revascularization. Weintraub et al. (52) reported mortality results after PCI, linking PCI data from the CathPCI National Cardiovascular Data Registry (NCDR) to the Centers for Medicare and Medicaid Services (CMS) database. In this study of 343,466 patients aged ≥65 years undergoing first PCI in the CathPCI Registry, a high early phase hazard of death was observed in survival curves in patients with LVEF <0.30. Similarly, Shahian et al. (53) reported mortality results in 348,341 isolated CABG patients ≥65 years of age, linking data from the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database to the CMS database. Early mortality risk was also evident in patients with LVEF <0.30. The proportion

of the high mortality risk in the first few months after revascularization that is due to arrhythmic death is unknown. Nonrandomized, retrospective studies, however, have suggested a benefit of ICD implant early after coronary revascularization (54–57).

The WCD may play a role in patients at risk of sudden cardiac death in the early period after revascularization. In a recently published retrospective evaluation of 4958 patients with EF ≤0.35 after CABG and PCI from two combined databases, 809 patients who were discharged with a WCD were compared to the remaining 4149 patients (58). The WCD was associated with a lower 90-day mortality in patients after CABG (no WCD: 7% vs WCD: 3%) and after PCI (no WCD: 10% vs WCD: 2%). For the entire WCD group, 18 appropriate defibrillations occurred in 11 patients (12% of patients discharged with a WCD). Inappropriate shocks accounted for 42% of the therapies delivered.

An electrophysiologic study with programmed stimulation may play a role in identifying patients at risk of developing sustained ventricular tachyarrhythmias after revascularization, although the results from small observational studies have been mixed. In an observational study of 109 consecutive patients who had NSVT 2-66 days after PCI or CABG with a mean ejection fraction of 0.30, sustained monomorphic VT was induced in 42% of patients and an ICD was implanted (55). During a mean follow-up of 27 months, 33% of patients with an ICD had appropriate therapy, and more relevant to this discussion, 16% of patients developed VT/VF or sudden cardiac death in the first year of follow-up. In another retrospective study of 69 patients who received an ICD within 4 months of surgery, inducible ventricular tachyarrhythmia was not identified as a variable for predicting appropriate ICD therapy or mortality, although the numbers were small (54).

The rationale for waiting 90 days after revascularization to implant an ICD is based upon the premise that LV function can improve sufficiently to raise the LVEF to above 0.35. It remains a major challenge to predict those patients who will or will not significantly improve their LV function. In patients with LV dysfunction before CABG, persistent LV dysfunction after CABG with LVEF ≤0.35 has been reported in 25%-74% of patients (54,57). In one recent study of patients with reduced LVEF (<0.40) undergoing CABG, 30% of patients had improvement in left ventricular function, although only 6% had an improvement of ≥0.05 units on repeat assessment 9-12 months after revascularization (59). Various preoperative imaging studies can predict improvement in postoperative LVEF and survival outcomes in patients who have significant regions of ischemic or hibernating but viable myocardium and who are adequately revascularized (60,61). However, in the Surgical Treatment for Ischemic Heart Failure (STICH) trial, identification of viability preoperatively failed to identify patients with a differential survival benefit from CABG as compared to medical therapy alone (62). Nonetheless, imaging studies have shown utility for predicting arrhythmias; several single-center studies have demonstrated that cardiac Magnetic Resonance Imaging (MRI) incorporating late gadolinium enhancement (LGE-CMR) can assess and quantify myocardial scars and predict future ventricular tachyarrhythmias, including appropriate ICD therapies in both primary and secondary prevention patients (63–67). If improvement of LVEF is suspected on clinical grounds, repeat imaging prior to ICD implantation can provide important information for the decision process. Since institutions and specific methods for measuring LVEF vary, similar techniques should be used when possible if serial measurements of the LVEF are required.

There is high early mortality demonstrated in patients with low LVEF despite coronary revascularization. Thus, in patients who previously qualified for the implantation of an ICD for primary prevention of sudden cardiac death and who have undergone revascularization that is unlikely to result in an improvement in LV ejection fraction >0.35, and who are not within 40 days after an acute MI, implantation of an ICD can be useful (**Figure 4**).

Patient Population #8B: *Patients within 90 days of revascularization who have previously satisfied criteria for implantation of a secondary prevention ICD (resuscitated from cardiac arrest due to VT/VF).*

Recommendations:

- In patients within 90 days of revascularization who have previously qualified for the implantation of an ICD for secondary prevention of sudden cardiac death (resuscitated from cardiac arrest due to ventricular tachyarrhythmia) and have abnormal left ventricular function, implantation of an ICD *is recommended.*
- In patients within 90 days of revascularization who have previously qualified for the implantation of an ICD for secondary prevention of sudden cardiac death (resuscitated from cardiac arrest due to ventricular tachyarrhythmia) that is unlikely related to myocardial ischemia/injury and have normal left ventricular function, implantation of an ICD *is recommended.*
- In patients within 90 days of revascularization who have previously qualified for the implantation of an ICD for secondary prevention of sudden cardiac death (resuscitated from cardiac arrest due to ventricular tachyarrhythmia) that was not related to acute myocardial ischemia/injury and who were subsequently found to have coronary artery disease that is revascularized with normal left ventricular function, implantation of an ICD *can be useful.*

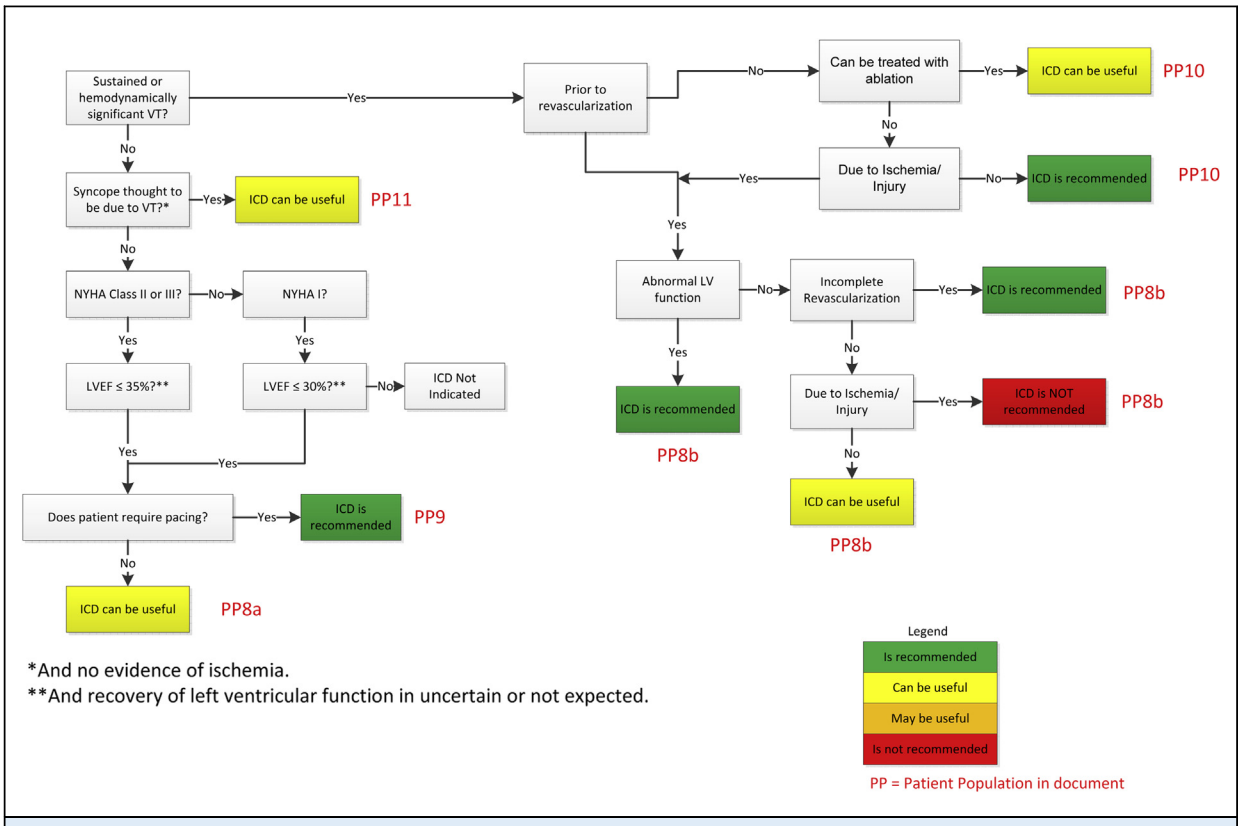

FIGURE 4 ICD Implantation Within 90 Days of Revascularization

ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VT = ventricular tachycardia.

- In patients within 90 days of revascularization who were resuscitated from cardiac arrest due to ventricular tachyarrhythmia that was related to acute myocardial infarction/injury, with normal left ventricular function, and who undergo complete coronary revascularization, an ICD is *not recommended*.

Discussion: Patients who met ICD implant criteria for secondary prevention of sudden cardiac death (resuscitated from pulseless VT or VF) prior to coronary revascularization are likely to remain at high risk after revascularization unless the initial ventricular tachyarrhythmia event was clearly related to an acute MI and treated with complete revascularization of the ischemic region with complete normalization of LV function. In patients resuscitated from cardiac arrest that was not in the setting of an acute MI or in the setting of myocardial scarring, there is likely to remain a myocardial substrate that is vulnerable to recurrent ventricular tachyarrhythmias following revascularization, even if the LVEF were to improve to >0.35. In the AVID trial, 10% of ICD patients and 12% of patients randomized to drugs underwent coronary revascularization, and revascularization did not alter survival (3). This outcome is supported by an analysis of patients in the AVID Registry, who had life-threatening ventricular tachyarrhythmias due to transient or correctable causes. The majority of such patients were regarded as having myocardial ischemia as a correctable cause and underwent revascularization as primary therapy, yet still remained at high risk of death in follow-up, with mortality no different or perhaps even poorer than that of the primary ventricular tachyarrhythmia population randomized in the main AVID study (68). In another analysis of the AVID Registry, both revascularization and ICD implantation improved survival, but the survival benefit of an ICD was independent of revascularization (69). Nonrandomized observational or retrospective studies of ICD implantation early after revascularization in secondary prevention patients have also reported similar event rates to those of primary prevention studies, including early occurrence of ventricular tachyarrhythmias and appropriate ICD therapies (57,70–72). In an observational study of 58 patients who underwent CABG at the time of defibrillator implant, LVEF ≤0.30 was an independent predictor of defibrillator discharge (73). An earlier observational study showed survival in cardiac arrest survivors undergoing CABG (without ICD implant) to be excellent if LV function was

preserved (74). Therefore, in patients who have previously qualified for the implantation of an ICD for secondary prevention of sudden cardiac death (resuscitated from cardiac arrest due to ventricular tachyarrhythmia) likely related to myocardial ischemia/injury, and have abnormal left ventricular function, an ICD is recommended. If left ventricular function is normal and the cardiac arrest is likely related to myocardial ischemia/injury that is revascularized, implantation of an ICD can be useful. If the cardiac arrest is unlikely to be related to myocardial ischemia/injury, an ICD is recommended.

Patient Population #9: *Patients within 90 days of revascularization who also have an indication for PPM implantation.*

Recommendation:

- In patients within 90 days of revascularization who require nonelective permanent pacing, who would also meet primary prevention criteria for implantation of an ICD, and in whom recovery of left ventricular function is uncertain or not expected, implantation of an ICD with appropriately selected pacing capabilities *is recommended.*

Discussion: Approximately 1.5% of patients undergoing cardiac surgery will require a PPM prior to discharge (75–78). Known predictors include conduction abnormalities prior to surgery and type of surgery, including aortic valve replacement, tricuspid valve replacement, and atrial fibrillation surgery (75,79). In patients who require ventricular pacing, biventricular pacing may be needed if ventricular pacing is likely to exceed 40% in patients with an LVEF ≤0.35, in accordance with the 2012 ACC/AHA/HRS Update of the 2008 Guidelines for Device-Based Therapy as a Class IIa indication (8). Patients enrolled in the major biventricular pacing trials (Multicenter InSync ICD Randomized Clinical Evaluation [MIRACLE], MUltisite STimulation in cardiomyopathy [MUSTIC], Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure [COMPANION], Cardiac Resynchronization-Heart Failure [CARE-HF], and Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy [MADIT-CRT]) were primarily at least 3 months from prior revascularization (80–84). An exception was the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT), which allowed patients with recent revascularization; patients needed to be at least 1 month from revascularization (CABG or PCI) if the LVEF was >0.30, but could have more recent revascularization provided the LVEF was ≤0.30 (85).

However, when faced with the need for permanent pacing and the significant likelihood that revascularization will not result in an LVEF >0.35, the primary implantation of an ICD will avoid the need for a second procedure to upgrade a pacemaker to an ICD, which has been associated with a higher risk of complications (54,57). In the REPLACE prospective registry of complications after implanted cardiac device replacement or upgrades, major complications occurred in 4.0% of 1031 patients undergoing generator replacement and 15.3% of 713 patients undergoing device replacement/upgrades with addition of a lead (86). Major complications were higher with ICD compared with pacemaker generator replacements, and were highest in patients who had an upgrade to or a revised cardiac resynchronization therapy device (18.7%).

In patients who require urgent, nonelective permanent pacing following revascularization (CABG or PCI) within the past 90 days with an LVEF ≤0.35, an ICD is recommended. The choice of a single, dual, or biventricular system should be based upon the clinical setting, current guidelines and consensus statements that address this decision under general conditions, and patient preference (5,8,87).

Patient Population #10: *Patients within 90 days of revascularization who subsequently present sustained or hemodynamically significant ventricular tachyarrhythmia.*

Recommendations:

- In patients within 90 days of revascularization with structural heart disease and sustained (or hemodynamically significant) ventricular tachyarrhythmia that was not clearly related to acute myocardial infarction or ischemia, implantation of an ICD *is recommended*.
- In patients who, within 90 days of revascularization, develop sustained (or hemodynamically significant) VT that can be treated by ablation therapy, implantation of an ICD *can be useful.*

Discussion: The survival benefit of an ICD for patients with symptomatic sustained VT (not in the setting of cardiac arrest) specifically as a cause for syncope or associated with an ejection fraction below 0.40 has been previously demonstrated in the AVID trial (3). Symptomatic sustained ventricular tachycardia without cardiac arrest was also included in CIDS, while the Cardiac Arrest Study Hamburg (CASH) required all ventricular arrhythmias to be associated with cardiac arrest (33,88). As a result, the 2008 ACC/AHA/HRS Guidelines for Device-Based Therapy specify ICD implant as a Class I indication for patients with "structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable" (5). An additional Class IIa recommendation is made for ICD implant in patients with "sustained VT and normal or near-normal ventricular function" (5). It is important to note that the recommendations do not have any time constraints.

The question yet remains whether an ICD can provide further and independent survival benefit to patients with sustained ventricular tachyarrhythmias (not related to a cardiac arrest) who undergo revascularization. In a small, retrospective, single-center study that followed 93 patients with VT or VF felt to be due to myocardial ischemia and who underwent CABG, the long-term survival was excellent over 8 years at 88%, though survival was not compared between patients with and without an ICD (70). However, this conclusion is challenged by data from the AVID registry of patients not randomized to the main study (69). Wyse et al. (68) examined the long-term follow-up of patients in the AVID registry regarded to have VT or VF that was secondary to a transient or correctable cause, which was most commonly myocardial ischemia, comprising 65.8% of the 278 patients analyzed. Compared with a cohort of 2013 registry patients with out-of-hospital primary VT or VF, patients thought to have a correctable cause had a higher mortality after adjustment for covariates, including revascularization. This study did not separately analyze outcomes according to index arrhythmia.

Predictors of an appropriate ICD shock in relationship to revascularization were reported in a single-center retrospective study of 591 patients, of whom 73 patients had VT and 77 patients had syncope (89). These authors found in a multivariate analysis that HRs for ICD shock were lower in CABG patients, but higher in patients with left ventricular enlargement. The incremental benefit of an ICD for revascularized patients was best explored in another AVID registry substudy that analyzed a cohort of 2202 patients, of whom 281 patients underwent CABG after the index arrhythmic event (patients with PCI were excluded) (69). Ventricular tachycardia was the index event in 39% of revascularized patients and 58% of nonrevascularized patients ($p < 0.001$). ICDs were implanted more commonly in patients who were not revascularized (51% vs 42%, $p = 0.006$). Registry patients who underwent CABG had improved survival, with an adjusted HR of 0.67 ($p = 0.011$). However, an ICD gave a further survival advantage independent of revascularization. In this study as well, analysis according to the index arrhythmia was not made, but a large fraction of the patients studied had VT.

Patients with VT can be considered for EP study because VT may be completely treated by ablation therapy; in the situation where VT is treated by ablation, an ICD can still be considered, as recurrence rates can be high. In all other patients with structural heart disease and sustained (or hemodynamically significant) VT or VF that is not clearly related to acute MI, implantation of an ICD is recommended.

Patient Population #11: *Patients within 90 days of revascularization who present with syncope likely due to ventricular tachyarrhythmia.*

Recommendation:

- In patients within 90 days of revascularization present with syncope that is thought to be due to ventricular tachyarrhythmia (by clinical history or documented NSVT, or EP study), implantation of an ICD *can be useful.*

Discussion: The evaluation of patients with syncope can be challenging. Patients with NSVT pose concerns that syncope is due to sustained VT. However, even in patients with structural heart disease, syncope might still be nonarrhythmic in its etiology. Therefore, a careful evaluation of the syncope patient is needed. The presence of structural heart disease with reduced LV ejection fraction or inducibility for VT at EP study is highly suggestive that syncope is due to ventricular tachyarrhythmia.

Therefore, it is our recommendation that in patients with syncope that is likely due to ventricular tachyarrhythmia either by documentation of NSVT or inducible VT at EP study, implantation of an ICD can be useful regardless of the timing of past revascularization.

Patient Population #12: *Patients within 90 days of revascularization who have a previously implanted ICD that requires elective replacement due to battery depletion.*

Recommendation:

- In patients within 90 days of revascularization with an ICD that requires replacement due to battery depletion, after careful assessment of comorbidities and the current clinical situation, replacement of the ICD generator *is recommended.*

Discussion: The number of patients with an ICD in place at the time of cardiac surgery is currently unknown. However, with the increase in congestive heart failure, the number of ICD patients undergoing revascularization is likely to increase. No data exist regarding the risk of sudden cardiac death in patients with an ICD at its end of life within the first 90 days of revascularization, yet there remains the concern that the very early post-revascularization (PCI or CABG) time period is one of increased total mortality risk (52,53).

Therefore, we recommend that the ICD patient whose generator is at its end of service due to battery depletion undergo generator replacement regardless of the timing of revascularization.

Patient Population #13: *Patients within 90 days of revascularization who are also listed for heart transplantation or who undergo implantation of a ventricular assist device.*

Recommendation:

- In patients within 90 days of revascularization who have been listed for heart transplant or implanted with

a ventricular assist device, and who are not within 40 days of an acute myocardial infarction, implantation of an ICD *can be useful.*

Discussion: The ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy specify a Class IIa indication for the implantation of an ICD in nonhospitalized patients who are awaiting heart transplantation (5). It is a Class III indication by those guidelines if patients are NYHA Class IV with drug-refractory heart failure and are not candidates for transplant or biventricular pacing. The exclusion to allow an ICD in the setting of biventricular pacing is due to the inclusion of ambulatory Class IV heart failure patients in the COMPANION trial who improved in functional status and survival with CRT-D therapy (82). In the recent 2012 update, it is now a Class I recommendation to implant a biventricular ICD in ambulatory Class IV patients with LBBB and QRS duration ≥150 ms (8).

Patients who are considered candidates for transplant pose other considerations. However, it is implicit in the listing for the transplant that there are no other treatments that have been successful or that are expected to meaningfully reverse the patient's status, including revascularization. Even if revascularization has been performed in the recent past, the listing for transplant should be taken as implying that revascularization was inadequate or failed.

The literature relating to the benefit of ICD implants in patients awaiting transplant include observational retrospective analyses from single centers from the 1990s and early 2000s showing improved survival for patients awaiting transplant with an ICD, with survival curves separating within the first 3 months (36–39). In an analysis of 310 patients awaiting transplant at the University of Minnesota, the overall mortality in ICD patients was 22% compared with 60.2% in non-ICD patients, and both ICD implant and beta-blockade were protective (38). Survival at 6 months and at 1, 2, 3, and 4 years was significantly improved in ICD patients ($p = 0.0001$). In an analysis of 854 patients awaiting transplant in Europe and with a median follow-up of 4.7 months, total mortality in ICD patients was 11.8% compared with 21.5% in non-ICD patients ($p = 0.03$) (39). Of note, the indication for ICD implant in these studies was largely for secondary prevention.

In recent years, literature on large cohorts of patients with VADs has emerged (90,91). Many of these patients are awaiting transplant, but an increasing proportion receive assist devices as lifetime therapy or to allow further time to determine eligibility for transplantation. The first postoperative month is recognized as a period of increased risk of ventricular tachyarrhythmias (92,93). However, the risk of ventricular arrhythmias persists beyond this immediate postoperative period, and in an observational study of 478 VAD patients from the Cleveland Clinic, of whom 90 patients had an ICD, one-third of patients had their first arrhythmic event beyond 30 days postoperation (90). Furthermore, survival was improved in ICD patients ($p = 0.024$), and they were more likely to survive to transplant ($p = 0.015$). Survival curves in these studies separate early between ICD and non-ICD patients, within the first 3 months. Of note, the majority of patients in these studies received a left ventricular assist device (LVAD), and the arrhythmic risk and protection afforded by an ICD can be attenuated in patients with a biventricular assist device (BIVAD) (91).

The LVAD confers some protection from hemodynamic collapse during ventricular tachycardia or fibrillation. However, the lack of adequate right ventricular function compromises filling of the left ventricle and the assist device. Although death with VT or VF is less likely than without LVAD support, syncope can occur, sometimes with significant head injury. Demonstration of better survival with ICDs in the VAD patients from observational studies might reflect in part the better prognosis for patients with ICDs for chronic heart failure than for patients with new acute hemodynamic collapse leading to urgent VAD placement. Patients with a BIVAD generally tolerate even ventricular fibrillation and are unlikely to derive survival benefit from an ICD prior to transplant.

In light of the demonstrated improved survival with an ICD, particularly emerging within the first few months, we consider an ICD implant to be useful in outpatients awaiting transplant or with a VAD who are not <40 days from MI. Since revascularization in such patients is implied to have been unsuccessful, the timing of any recent revascularization should not be a deterrent to the implantation of an ICD.

7. ICD IMPLANTATION <9 MONTHS FROM THE INITIAL DIAGNOSIS OF NONISCHEMIC CARDIOMYOPATHY

Patient Population #14: *Patients <9 months from the initial diagnosis of nonischemic cardiomyopathy (NICM) who have significant left ventricular dysfunction and heart failure symptoms.*

Recommendations:

- Implantation of an ICD for primary prevention *is not recommended* within the first 3 months after initial diagnosis of NICM.
- If recovery of left ventricular function is unlikely, implantation of an ICD for primary prevention *can be useful* between 3 and 9 months after initial diagnosis of NICM.

Discussion: Historically, before the widespread use of many established therapies, the 5-year mortality for NICM

was estimated to be 50%, and 30% of the deaths were sudden (4,6). Although ventricular tachyarrhythmias are the most common cause of sudden death, bradycardia and pulseless electrical activity can also cause sudden death, particularly in those patients with advanced disease (94). The primary challenge in deciding whether or when to implant an ICD is distinguishing between patients who are recently diagnosed with previously unrecognized chronic cardiomyopathy and those patients whose cardiomyopathy is truly of recent onset. The initiation and titration of optimal medical therapy often improves LVEF out of range of primary ICD indications, but this is particularly true for patients with less than 6 months of disease (**Table 3**). In the Intervention in Myocarditis and Acute Cardiomyopathy (IMAC)-2 study, 373 patients with new-onset cardiomyopathy (LVEF ≤0.40, <6 months from initial diagnosis) were followed for 4 years (95). Transplant-free survival at 4 years was 88%, and mortality at 4 years was 4%. In addition to improved survival, 70% of patients had an absolute increase in LVEF of 10%, and 25% of patients had complete or near-complete (LVEF >0.50) resolution of their cardiomyopathy. Approximately one-third of the deaths were sudden, and eight patients were hospitalized for ventricular arrhythmias during the follow-up period. In the Marburg Cardiomyopathy Study, 343 patients with NICM from a single center were followed for more than 4 years. During the study period, 33 patients (13%) died and 10 patients (4%) underwent cardiac transplant (96). Major arrhythmic events, defined as sustained VT, VF, or sudden cardiac death, were observed in 46 patients (13%). LVEF was the only significant independent risk factor for a major arrhythmic event, with each 10% decrease in EF associated with a 2.3 fold increase in risk. A later subanalysis of the data suggested that longer episodes of NSVT (≥10 beats) were associated with a higher risk of major arrhythmia events (no NSVT: 2% per year; 5- to 9-beat runs of NSVT: 5% per year; ≥10 beat runs of NSVT: 10%; $p < 0.05$) (97).

Four randomized studies have evaluated the use of ICDs in patients with NICM (1,16,98,99). The two largest trials, the DEFINITE trial and the SCD-HeFT, showed a decrease in arrhythmia-related death associated with ICD use (1,16). Two smaller randomized studies on ICD use in NICM were performed before DEFINITE and SCD-HeFT. In the Cardiomyopathy Trial (CAT), 104 patients with newly identified NICM (within 9 months of initial diagnosis) and Class II/III heart failure were randomized to ICD therapy or no ICD therapy (98). The initial assumptions used for trial design included a 30% mortality rate at 1 year, and a 1-year 6% absolute benefit from ICD therapy. The actual observed 1-year mortality rate was only 6% in the first 104 patients, and the trial was stopped prematurely. In the Amiodarone Versus Implantable Cardioverter-Defibrillator Randomized Trial (AMIOVIRT), 103 patients with NICM (LVEF ≤0.35) and NSVT were randomized to ICD therapy or amiodarone (99). The study was stopped prematurely, in this case because the prospective rule for futility was reached. There was no difference in survival between the two therapies (amiodarone 1-year survival: 90% vs ICD 1-year survival: 96%). There was no specific time from initial diagnosis to enrollment in AMIOVIRT, although the average duration of NICM was 3 years prior to enrollment into the trial.

TABLE 3 Relevant Studies in NICM

Natural History of SCD in NICM Grimm et al. (MACAS) (96)	• 343 patients with EF <0.45 and an LVEDD >56 mm followed for 52 months • Overall sudden death rate of 6.7% • At 9 months, arrhythmia-free survival and transplant-free survival of approximately 5% for LVEF <0.30 and 2%–3% for LVEF >0.30
McNamara et al., Sheppard et al. (IMAC-2) (95,102)	• 373 patients with LVEF <0.40 for less than 6 months • At 6 months, 92% on an ACEI, 94% on a BB, and 20% with an ICD • At 6 months, 70% had an absolute increase in EF by >10 EF "units" and 39% had an increase of 20 U • At 6 months, 40% with an EF >0.45 and 25% with a normal EF • No difference in mortality with the ICD Rx • Six patients with sudden death at a mean 420 days (range 23–1059 days)
Zecchin et al. (103)	• Analysis of 503 patients from the Heart Muscle Registry of Trieste initially evaluated between 1988 and 2006 • Complete data on 287 patients • 245 with EF ≤0.35 and ≥Class II NYHA heart failure symptoms • 31% remained with EF ≤0.35 and NYHA symptoms after Rx and 5 months f/u • 227 with EF >0.35 or Class I NYHA heart failure • 10% had progression to EF <0.35 and increased symptoms • 2% sudden death rate between initial visit and follow-up in both groups
Effect of Timing of ICD Implantation Kadish et al. (100)	• 458 patients with NICM, EF <0.36 and unsustained ventricular arrhythmias • 150 patients <3 months from diagnosis to randomization, 66 between 3 and 9 months, and 242 >9 months • Similar ICD benefit regardless of the time between diagnosis and randomization
Makati et al. (101)	• 131 patients with NICM divided into two cohorts: <9 months vs >9 months from symptom onset • ICD treated arrhythmias in 27% in both groups

ACEI = angiotensin converting enzyme inhibitor; BB = beta blocker; ICD = implantable cardioverter-defibrillator; IMAC = Intervention in Myocarditis and Cardiomyopathy; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; MACAS = Marburg Cardiomyopathy Study; NICM = nonischemic cardiomyopathy; NYHA = New York Heart Association.

All three of the current guidelines that address the use of ICD therapy for primary prevention of sudden cardiac death in NICM (ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death, ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy, and the 2009 Focused Update of the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure) are consistent and recommend ICD therapy for patients with NICM, Class II or III heart failure, and an LVEF ≤0.35 (4–6). None of the guidelines have a time constraint on the duration of nonischemic cardiomyopathy, but the 2006 Ventricular Arrhythmias Guideline emphasize the importance of "chronic optimal medical therapy" and the 2008 Guidelines for Device-Based Therapy emphasize that reversible causes for transient left ventricular function be excluded, response to optimal medical therapy be assessed, and that "physicians should consider the timing of defibrillator implantation carefully" (6). The 2013 Appropriate Use Criteria for ICD Therapy are more expansive and classify ICD therapy as "appropriate" in NICM >3 months on guideline-directed therapy for LVEF ≤0.40 in the setting of NYHA Class I-III symptoms, and "may be appropriate" ≤3 months in patients with LVEF ≤0.30 and NYHA Class II or III symptoms (9).

The relationship between the benefit of ICD implantation and the duration of NICM has been evaluated in several studies. In the DEFINITE study, the average duration of NICM prior to randomization was almost 3 years (16). In a subsequent subanalysis that compared outcomes between patients with ≤3 months' duration (n = 150) vs patients >3 months' duration (n = 308), and between patients ≤9 months (n = 216) vs patients >9 months (n = 242), the investigators found similar benefits associated with ICD implant regardless of duration of NICM (100). It is important to note that patients were not randomized in the trial if they were thought to have a potentially reversible cause of cardiomyopathy such as peripartum cardiomyopathy, myocarditis, or acute drug-induced cardiomyopathy. Similarly, in a single-center study of 131 patients with NICM and ICDs, a similar frequency of arrhythmias appropriately treated with ICDs was found in the 52 patients with diagnosis of NICM <9 months (27%) when compared with the 79 patients with NICM ≥9 months (27%) (101). In contrast, in a subanalysis of IMAC-2, early ICD placement did not have an impact on survival (102).

Analysis of the IMAC-2 patient cohort emphasizes the dynamic nature of left ventricular function in some patients with the recent diagnosis of NICM. Similarly, in a cohort from an Italian registry of 245 patients with newly identified NICM who would qualify for an ICD on the basis of symptoms and ejection fraction, 109 patients demonstrated improvement in their left ventricular function at the 9-month follow-up (103). It might be that even with improvement in left ventricular function, patients remain at risk of ventricular arrhythmias. In a recently published subanalysis of the DEFINITE trial, 187 patients had a follow-up echocardiography for assessment of left ventricular function (104). Of these, 96 patients (51%) had an absolute improvement in LVEF >5%, 79 patients (42%) had no change in LVEF, and 12 patients (6%) had an absolute decrease in LVEF >5%. Patients with improvement in LVEF had significant improvement in survival when compared with patients with no change in LV function (HR: 0.22; 95% CI: 0.06–0.82; p = 0.023) and worsening LV function (HR: 0.09; 95% CI: 0.02–0.39; p = 0.001). In addition, patients with improved LV function had fewer arrhythmic events (HR: 0.47; 95% CI: 0.22–1.02; p = 0.049), but 5.7% of patients had significant ventricular tachyarrhythmias even after the ejection fraction improved to >0.35.

Separating patients who will have improvement in left ventricular function, a decrease in overall mortality, and a decreased risk of sudden death from those patients with irreversible or progressive left ventricular dysfunction is difficult. In the IMAC-2 study, at initial evaluation, smaller left ventricular end-diastolic diameter, higher systolic blood pressure, and an acute inflammatory process identified at biopsy were associated with an increased likelihood of recovery of left ventricular function (95). Conversely, black race and higher NYHA functional class were associated with a lower EF at follow-up. Myocardial fibrosis in the mid-wall of the left ventricle identified by magnetic resonance imaging might provide some additional prognostic information on the potential reversibility of cardiomyopathy (105). In a cohort of 472 patients, 142 patients (30%) had mid-wall fibrosis, and during a median follow-up of 5.3 years, these patients had a higher risk of mortality (HR: 2.96; 95% CI: 1.87–2.96) and a higher risk of sudden death (HR: 4.61: 95% CI: 2.75–7.74; p < 0.001) (104). Genetic testing can also play a role in risk stratification of patients with NICM (105). Preliminary studies suggest that NICM due to LMNA, TNNT2, SGCD, RBM20, and CHRM2 mutations can be at higher risk of sudden cardiac death (106–110). Patients with cardiac sarcoidosis and LVEF <0.30 are unlikely to improve with medical therapy (111). Giant cell myocarditis is a rare cause of myocarditis characterized by large multinucleated cells and has an extremely virulent course that does not respond to therapy (112).

Taken collectively, the data suggest that a significant proportion of patients with the new diagnosis of NICM will have improvement in left ventricular function, but some patients will remain at risk of ventricular arrhythmias. The clinician must carefully evaluate those patients with relatively recent onset NICM, and ICD implantation for primary prevention between 3 and 9 months can be useful

in selected patients with NICM who are unlikely to have recovery of left ventricular function. Patients with sarcoidosis, giant cell myocarditis, or familial cardiomyopathy with a family history of sudden death might benefit from ICD implantation during this period. The improvement in left ventricular function found in the IMAC-2 study emphasizes the importance of aggressive appropriate medical treatment. In patients with NICM <9 months it is generally prudent to delay ICD until the full effect of medical therapy can be evaluated. Implantation of an ICD is not recommended within the first 3 months after the initial diagnosis of NICM unless other potential reasons for ICD implant are present (populations 15-18) (Figure 5).

Patient Population #15: *Patients <9 months from the initial diagnosis of NICM who meet criteria for primary prevention ICD who also have an indication for PPM implantation.*

Recommendation:

- In patients <9 months from the initial diagnosis of NICM who require nonelective permanent pacing, who would meet primary prevention criteria for implantation of an ICD, and recovery of left ventricular function is uncertain or not expected, implantation of an ICD with the appropriately selected pacing abilities *is recommended*.

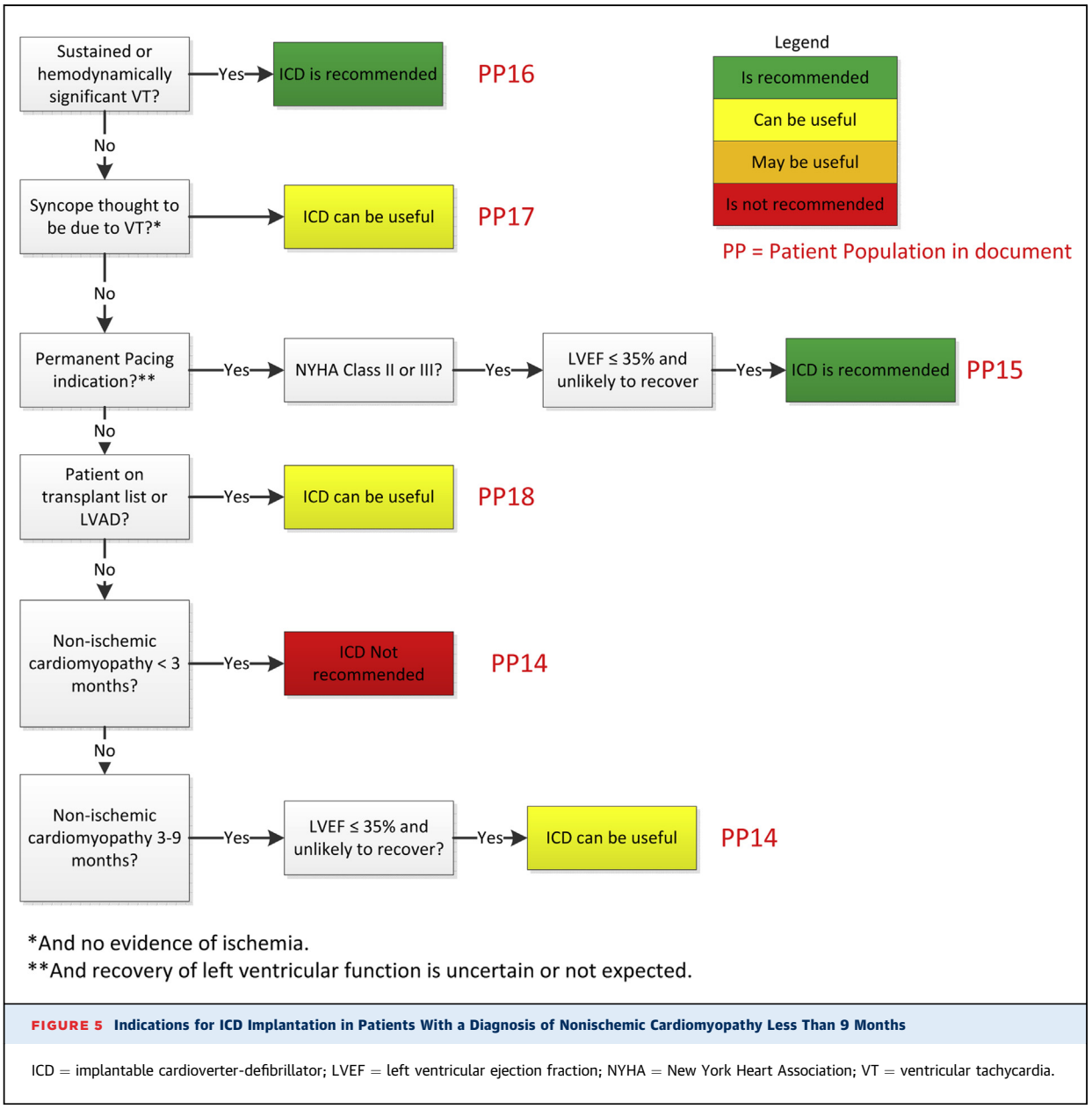

FIGURE 5 Indications for ICD Implantation in Patients With a Diagnosis of Nonischemic Cardiomyopathy Less Than 9 Months

ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VT = ventricular tachycardia.

Discussion: Some patients can develop NICM and atrioventricular (AV) conduction abnormalities over a relatively short time. Muscular dystrophies are a group of inherited disorders of skeletal muscles with diverse presentations that can sometimes confront the clinician with difficult decisions. Duchenne, Becker, and limb-girdle types 2C-2F and 2I are associated with dilated cardiomyopathy and increased risk of ventricular tachyarrhythmias, and are associated with progressive AV conduction disorders that are generally proportional to the amount of left ventricular dysfunction present (107). Patients with myotonic dystrophy Type 1 also can present with cardiomyopathy and progressive AV block. In the largest registry published to date, 406 patients with genetically confirmed myotonic dystrophy were followed for 9.5 years (108). Forty-six patients received pacemakers for conduction abnormalities and 21 patients received ICDs primarily for LV dysfunction. During follow-up, seven patients in the pacemaker group had sudden cardiac death and 6.5% of patients had sudden death due to ventricular tachyarrhythmias compared with no patients in the group who received ICDs.

Mutations of the lamin A/C (LMNA) gene can be associated with a variety of cardiac abnormalities such as cardiomyopathy, atrial and ventricular tachyarrhythmias, and conduction tissue disease; and extracardiac manifestations such as skeletal muscle abnormalities and premature aging. In an early small series of 19 patients with LMNA gene mutations who were initially referred for pacemaker implantation and who underwent ICD implantation, during a mean follow-up of 34 months, 42% of patients received appropriate ICD therapy (109). No factor, including LVEF, presence of spontaneous or inducible ventricular tachyarrhythmias, or drug therapy, was associated with appropriate ICD therapy. In a recently published multicenter cohort of 269 patients with LMNA mutations, approximately 35%-40% had cardiomyopathy (EF <0.45) and almost 50% had AV block (113). In the 152 patients who did not have an ICD, sudden death occurred in 13 patients (9%) compared to 1 of 117 patients who received ICDs. Twenty-eight of 117 patients (24%) received appropriate ICD therapy.

Patients with cardiac sarcoidosis or giant cell myocarditis can also present with AV block. In a single-center evaluation of 133 patients aged 18-55 who underwent pacemaker implantation for a second- or third-degree AV block, 18 patients (14% of the entire cohort and 25% of patients with unexplained AV block) had cardiac sarcoidosis or giant cell myocarditis and had an average LVEF of 0.52 with a range of 0.25-0.70 (114). During an average 4-year follow-up, LVEF decreased (0.43, range 0.15-0.65), and from this original group, 4 died, 4 had VF, 6 had sustained VT, and 1 patient underwent transplant for recurrent uncontrollable ventricular tachyarrhythmias.

No patients in the IMAC-2 trial presented with concomitant AV block, although 20% presented with LBBB (92). The ACC/AHA/HRS 2008 Device-Based Guidelines provide recommendations for pacing system implantation, and the ACC/HRS 2012 Consensus Statement on Pacing Mode provides information on appropriate pacing mode (5,87). To reduce the morbidity associated with possible additional procedures, for patients with the recent diagnosis of NICM (<9 months) who also have an urgent and nonelective indication for permanent pacing, initial implantation of an ICD with appropriate pacing capabilities is recommended, particularly in the presence of accompanying AV block.

Patient Population #16: *Patients <9 months from the initial diagnosis of NICM who also have sustained or hemodynamically significant ventricular tachyarrhythmia.*

Recommendation:

- In patients <9 months from the initial diagnosis of NICM with sustained (or hemodynamically significant) ventricular tachyarrhythmia, implantation of an ICD *is recommended*.

Discussion: Patients who present sustained or hemodynamically significant ventricular tachyarrhythmias in the setting of NICM are at high risk for a subsequent event. In a small study of 54 patients with NICM who received an ICD for sustained VT or sudden cardiac death, during 32-month follow-up, 28 patients (52%) received appropriate ICD therapy (115). In this cohort, 21 of 28 patients had therapy for VF, and the average time between ICD implant and first appropriate therapy was 9 months.

ICD therapy is beneficial in patients who have sustained or hemodynamically significant ventricular tachycardia with NICM <9 months. The clinical guidelines do not include time constraints for secondary prevention ICD implantation (**Table 1**).

Patient Population #17: *Patient <9 months from the initial diagnosis of NICM who present with syncope likely due to ventricular tachyarrhythmia.*

Recommendation:

- In patients <9 months from the initial diagnosis of NICM with syncope that is thought to be due to a ventricular tachyarrhythmia (by clinical history or documented NSVT), implantation of an ICD *can be useful*.

Discussion: Single-center studies have evaluated the natural history of patients with syncope in the setting of NICM (116,117). In a single-center study performed two decades ago, of 491 patients with advanced heart failure due to coronary artery disease (48%) and NICM (51%), 60 patients (12%) had syncope (116). During a mean follow-up of 1 year, the incidence of sudden death was higher in the syncope group compared with those patients without

syncope (syncope: 45% vs no syncope: 12%; $p < 0.00001$). In another single-center study that compared 108 patients with syncope in the setting of NICM with 71 patients who had NICM and sustained ventricular tachyarrhythmias, no differences in overall survival or risk of ventricular arrhythmias could be identified, and the risk of developing ventricular tachyarrhythmias was 26%–41% (117).

Unfortunately, traditional methods for risk stratification are generally less useful in patients with NICM. The ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death note that: "In DCM (dilated cardiomyopathy), EP testing plays a minor role in the evaluation and management of VT. This recommendation is related to the low inducibility, low reproducibility of EP testing, and low predictive value of induced VT" (6).

The ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death and the ACC/AHA/HRS 2008 Guidelines on Device-Based Therapy are consistent and provide a Class IIa recommendation for ICD therapy in patients with unexplained syncope and left ventricular dysfunction in the setting of NICM (5,6). The ACC/AHA/ESC 2006 Ventricular Arrhythmias Guidelines further stipulate that the patient must be receiving "chronic optimal medical therapy" and have a "reasonable expectation of survival with a good functional status for more than 1 year" (6).

Patient Population #18: *Patients <9 months from the initial diagnosis of NICM who are also listed for heart transplantation or who undergo implantation of a ventricular assist device.*

Recommendation:

- In patients <9 months from the initial diagnosis of NICM who have been listed for heart transplant or implanted with a left ventricular assist device, implantation of an ICD *can be useful*.

Discussion: There are scant data on the use of ICDs in patients with the recent diagnosis of NICM who have been listed for heart transplant or have a left ventricular assist device. The previously reviewed trials on the use of ICDs as a bridge to transplant (population 13) generally were equally distributed between patients with ischemic cardiomyopathy and NICM and have not shown a difference in the benefit of ICD based on etiology of cardiomyopathy. In one single-center study of 61 patients who received LVADs, sustained ventricular arrhythmias occurred in 43% of patients and were more likely to be observed in patients with NICM (approximately 60%) (118). The LVAD can be used as a bridge to recovery in some patients with NICM. In IMAC-2, an LVAD was used in 14 patients (3.8%), and in 8 patients the LVAD was used as a bridge to recovery (119). In this group of patients, LVEF improved from 0.20 at baseline to 0.49 at the 6-month follow-up.

The ACC/AHA/HRS 2008 Guidelines on Device-Based Therapy give a Class IIa recommendation for ICD implantation in nonhospitalized patients awaiting transplantation (5). Given the results of the retrospective studies and the subanalysis of IMAC-2, ICD therapy can be useful for patients who have had recently identified NICM (<9 months) who have been listed for transplant or who have undergone LVAD implantation and will be discharged from the hospital.

8. DUAL-CHAMBER VS SINGLE-CHAMBER ICD RECOMMENDATIONS

Recommendations:

- In patients with symptomatic sinus node dysfunction, an atrial lead *is recommended*.
- In patients with sinus bradycardia and/or AV conduction disturbances limiting the use and/or up-titration of necessary beta-blocker or other negative chronotropic drug therapy, an atrial lead *is recommended*.
- In patients with sinus rhythm who have a documented second- or third-degree AV block, but who are not otherwise candidates for cardiac resynchronization therapy, an atrial lead *is recommended*.
- In patients with bradycardia-induced or pause-dependent ventricular tachyarrhythmia (such as patients with long QT syndrome and torsades de pointes) an atrial lead *can be useful*.
- In patients with a documented history of atrial arrhythmias (but not in permanent atrial fibrillation), an atrial lead *may be considered*.
- In patients with hypertrophic cardiomyopathy and a significant resting or provocable left ventricular outflow tract gradient, an atrial lead *may be considered*.
- In patients with no documented history of atrial arrhythmias who have no other reason for requiring an atrial lead, an atrial lead *is not recommended*.
- In patients with permanent or longstanding persistent atrial fibrillation in whom efforts to restore or maintain sinus rhythm are not planned, an atrial lead *is not recommended*.
- In patients with conditions likely to result in VF (rather than monomorphic or polymorphic VT) without a bradycardia-induced or pause-dependent mechanism of initiation and no other indication for an atrial lead, an atrial lead *is not recommended*.

VF is the arrhythmia anticipated in conditions such as idiopathic ventricular fibrillation, Brugada syndrome, catecholaminergic polymorphous ventricular tachycardia, and short QT syndrome.

For every patient receiving an ICD in whom cardiac resynchronization therapy is either not indicated or not desired, physicians must choose to implant either a single-chamber ICD or a dual-chamber ICD. The published scientific evidence addressing this specific question, however, is limited. Current clinical guideline documents do not provide specific recommendations as to how physicians should proceed. Whereas the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Pacemakers and Antiarrhythmia Devices stated that a "dual-chamber pacemaker-ventricular defibrillator device is an appropriate choice for an ICD candidate who has a concomitant need for dual-chamber pacing or a patient with supraventricular tachycardia thought likely to lead to inappropriate ICD therapies," all reference to selection of single-chamber or dual-chamber ICDs was removed from the ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities (5,120). Given the limited evidence and lack of professional society guideline recommendations, wide variation in practice has emerged, ranging from some centers implanting no dual-chamber ICDs and some centers choosing to implant only dual-chamber ICDs (121). The next section reviews the scientific evidence underlying the current recommendations in this document regarding implantation of an atrial lead in patients receiving an ICD.

8.1 Randomized Trial Evidence from the Major Efficacy Trials of ICD Therapy

The vast majority of the nearly 5000 patients enrolled in the trials that established the efficacy of ICDs for the secondary prevention and primary prevention of sudden cardiac death received single-chamber ICDs (1,3). A notable exception, however, was the MADIT-II trial, in which nearly 44% of patients (313/717) received dual-chamber devices by physician choice (2). It is important to note that among patients randomly assigned to receive an ICD, selection of a single- or dual-chamber device was not randomized. In a subsequent substudy of MADIT-II, patients receiving dual-chamber devices had wider QRS complexes by electrocardiography, greater burden of comorbidity, and were older than the patients who received single-chamber devices (122). There were no significant differences in heart failure hospitalization, mortality, or risk of inappropriate shocks between those who received single- or dual-chamber ICDs.

8.2 Benefits of Dual-Chamber ICDs

The addition of an atrial lead to an ICD system provides several potential benefits. Dual-chamber devices can provide atrial pacing to patients with sinus node dysfunction or in the setting of other needs for atrial and/or dual-chamber pacing. In a recent analysis of the NCDR ICD database, less than 5% of ICD implants were placed for patients with a second- or third-degree AV block, and 12% were placed for bradycardic arrest (123). Pacing can be useful, for example, in selected patients with hypertrophic cardiomyopathy, myotonic dystrophy, cardiac sarcoidosis, infiltrative cardiomyopathies, and long QT syndrome. In particular, atrial or dual-chamber pacing receives a Class I recommendation for patients with long QT syndrome in the recently published consensus document on pacemaker mode selection (87). Initial placement of an atrial lead will reduce the likelihood and associated morbidity of a future upgrade procedure if sinus node dysfunction develops. The addition of an atrial lead allows for the use of dual-chamber arrhythmia discrimination algorithms and clearer clinical interpretation of device electrograms to differentiate ventricular and supraventricular arrhythmias, including the clear demonstration of ventriculoatrial dissociation during sustained monomorphic VT. Distinguishing monomorphic VT from supraventricular tachycardia presents challenges for clinicians caring for patients with ICDs. Rigorous studies, however, have had mixed results, demonstrating an improvement in arrhythmia discrimination and/or reduction in inappropriate therapies in some but not all studies (124–128). Placement of an atrial lead at the time of ICD implantation can also obviate the need for upgrade to a dual-chamber system in the future, should a need for atrial pacing arise. Goldberger and colleagues (129) found using a decision analysis model that the strategy of dual-chamber ICD selection in most patients made most sense, but this study assumed no increased risk with the addition of an atrial lead. In addition, the authors did not take into account the increased potential for lead failure and/or recall, and they also did not fully consider the shorter battery life of dual-chamber pulse generators. No randomized trial has clearly demonstrated a superiority of dual-chamber devices in terms of risk of inappropriate shocks, hospitalizations, or mortality.

8.3 Potential Risks of Dual-Chamber Device Selection

The addition of an atrial lead to an ICD system also poses several potential risks. Additional leads are associated with increased risk of dislodgement and other complications, including an increased risk of periprocedural mortality in dual-chamber ICD recipients compared with those who receive single-chamber devices (130,131). Battery life tends to be somewhat shorter in dual-chamber devices, which might lead to a greater need for generator replacement over patients' lifetimes. Additional leads can also present a theoretical risk of lead failure and/or recall, and in the event of infection or other factors that require lead extraction, additional leads present an incremental risk of vascular complications. Dual-chamber devices are also more expensive, because of both the additional lead

and the more complex pulse generator. On the other hand, upgrade procedures from single-chamber devices to dual-chamber devices incur both increased financial costs and the procedural risks to the patient that could be mitigated by implantation of a dual-chamber device as an upfront strategy (86).

Dual-chamber devices can also induce harm if strategies to minimize right ventricular pacing are not used. In the Dual-chamber and VVI Implantable Defibrillator (DAVID) trial, patients with decreased left ventricular systolic function and indications for ICD therapy received dual-chamber devices but were then randomly assigned to either VVI (single-chamber) or DDDR (dual-chamber with rate adaption) bradycardia pacing programming (132); in this trial, there was increased risk of the composite outcome of heart failure hospitalization plus mortality in the dual-chamber pacing arm, primarily in association with the greater proportion of right ventricular pacing with DDDR programming. In a subsequent subanalysis of DAVID, even patients with "soft indications" for pacing such as sinus bradycardia or first-degree AV block had poorer outcomes with the DDDR pacing (133). These risks of increased mortality and heart failure can be mitigated, however, with strategies to minimize or eliminate right ventricular pacing (134,135).

Even with the understanding that direct visualization of atrial electrograms can help clinicians to better distinguish sustained monomorphic VT in the care of individual patients, the increased risk of periprocedural complications and lack of clear benefit in rigorous studies in terms of hard clinical outcomes (such as incident inappropriate shocks, hospitalizations, or mortality) bring into question the practice of routine implantation of an atrial lead for the intended goal of improving discrimination of supraventricular arrhythmias from monomorphic VT, particularly in the era of modern programming strategies that have dramatically reduced the incidence of inappropriate therapies (133–136). In conditions where VF or polymorphic VT (rather than monomorphic VT) is the anticipated arrhythmia (such as idiopathic ventricular fibrillation, Brugada syndrome, short QT syndrome, and catecholaminergic polymorphic ventricular tachycardia), the value of an atrial lead would be even smaller.

8.4 Real-World Practice Patterns with Regard to Selection of Single-Chamber and Dual-Chamber ICDs

Although the majority of patients in the randomized trials of ICD therapy received single-chamber devices, and there is no randomized trial evidence demonstrating a superiority of the strategy of dual-chamber device selection, the majority of patients undergoing implantation of an ICD in the United States receive a dual-chamber device. After excluding those receiving cardiac resynchronization therapy devices, nearly two-thirds of all patients undergoing ICD implantation in the NCDR ICD Registry receive dual-chamber devices, and fewer than half of those receiving dual-chamber devices had clear bradycardia indications for dual-chamber pacing (123). In subsequent analyses excluding those patients with bradycardia indications for pacing, the preponderance of dual-chamber device selection persisted, but there was wide variation in practice patterns; some physicians and centers implanted no dual-chamber devices at all, and some implanted dual-chamber devices in all patients (121). This variation in practice strongly suggests a lack of consensus among practicing electrophysiologists regarding the best strategy for ICD device selection.

8.5 Device Selection in the Era of Modern Programming Strategies

Conventional ICD programming strategies have demonstrated incident appropriate therapies in more than 15% (MADIT-II) of cases, and incident inappropriate therapies in 10%–18% of cases in the first year after ICD implantation. However, modern programming strategies can dramatically reduce the incidence of both appropriate and inappropriate therapies. These strategies include minimization of right ventricular pacing, increased time from the onset of tachycardia until detection criteria are met, higher heart rate criteria than were conventionally employed to achieve arrhythmia detection, and more aggressive use of antitachycardia pacing (137–140). These strategies reduce the incidence of shocks, appropriate and inappropriate therapies, and, in the case of the Multicenter Automatic Defibrillator Implantation Trial: Reduce Inappropriate Therapy (MADIT-RIT), such strategies can also reduce mortality (137,138).

In MADIT-RIT, recipients of primary prevention ICDs were randomly assigned to either conventional ICD programming or to one of two strategies that employed modern programming techniques (137). The incidence of inappropriate therapies was 18% in the first year in the "conventional" arm, but with newer strategies, 5% or less received inappropriate therapies in the first year after device implantation.

These studies evaluating modern programming strategies are relevant to the decision to implant an atrial lead in patients undergoing implantation of an ICD for two important reasons. First, although all the patients in MADIT-RIT did have an atrial lead (as part of either a dual-chamber device or a cardiac resynchronization therapy defibrillator) to ensure definitive arrhythmia adjudication for study purposes, the programming strategies evaluated in the study can be equally employed in the absence of an atrial lead. Furthermore, with the dramatic reduction in the incidence of inappropriate therapies resulting from the use of these newer programming

strategies, the potential benefit of an atrial lead for enhanced arrhythmia discrimination might be reduced. Indeed, a preliminary report of the Use of Dual-chamber ICD With Special Programmed Features to Lower the Risk of Inappropriate Shock (RAPTURE) study found that in 100 patients randomized to either single-chamber or dual-chamber ICDs, the incidence of inappropriate therapies was 2% at 1 year for both groups (140).

9. DOCUMENTATION OF CLINICAL DECISIONS

In appropriately selected patients, ICD implantation is an important component for providing the best health care and improving survival. In both the MADIT-II and SCD-HeFT, the absolute mortality benefit after 3 years is 6%–9% (1,2). To put these data into perspective, chronic beta-blocker therapy after MI was associated with an absolute 2.5%–3.5% reduction in 3-year mortality in the Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) study and the Beta Blocker Heart Attack Trial (BHAT) (141,142). However, ICD therapy is expensive, and it is critical to choose patients who will benefit from implantation.

Documentation of the reasons for ICD implantation are essential for all patients, but even more critical for those patients who have not been represented in clinical trials because the potential survival benefit must be calculated by taking the additional risks of comorbid conditions into account. For example, for the patient in whom an ICD is being implanted within the 40-day window after myocardial infarction because of high-grade AV block and requirement for permanent pacing, it is essential for the clinician to document the clinical reasons behind the decision, particularly because two trials have demonstrated higher nonarrhythmia-related mortality associated with ICD placement during this time period (13,14). As suggested in the recommendations from this consensus statement, the clinician should document the urgent and nonelective requirement for ventricular rate support. In addition, once a decision to implant an ICD has been made, the clinician should also document the reasons for the pacing system that is implanted—single-chamber ICD, dual-chamber ICD, or an ICD with cardiac resynchronization capabilities. This decision must be made on the basis of previously published documents, the ACC/AHA/HRS 2008 Guidelines on Device-Based Therapy, the 2012 ACC/AHA/HRS Focused Update of this document, and the 2012 HRS/ACC Expert Consensus Statement on Pacemaker Device and Mode Selection (5,8,87). No clinical document can account for all possibilities. For example, selected patients with hypertrophic cardiomyopathy might benefit from ICD implantation, and ICD implantation within 90 days of revascularization might be appropriate in a patient with both hypertrophic cardiomyopathy and coronary artery disease (143). Again, the clinician should document the reasoning for ICD implantation.

The important and subtle distinctions of documentation must be understood by both health care providers and coding specialists. In a discussion of a hospital response to a United States Department of Justice audit, in an initial analysis of data from a single academic medical center, approximately 30% of patients were identified as possible inappropriate ICD recipients due to MI within the prior 40 days. However, on subsequent review of the medical record, the clinician responsible for the care of the patient and an independent reviewer both felt the abnormal troponin levels did not represent a myocardial infarction in 20% of the cases (144). In response to this finding, the coders at the institution received focused education and training on the clinical documentation, and a “same-day” peer review by all practicing electrophysiologists was instituted. In addition to these changes, the hospital instituted a routine quality assurance process that uses nursing staff evaluation of the medical record of patients who receive ICD implants. Peer review of patients undergoing ICD implantation is an important component of any quality improvement process. Good documentation is probably the best protection a clinician has against being cited for inappropriate ICD implantation and legal liability.

10. FUTURE RESEARCH AND DIRECTIONS

Clinicians should continue to support registries such as the NCDR for analysis of ICD implantation. The ICD component of the NCDR was implemented in 2005, and in the most recent published report, records from 850,000 ICD implants performed from registry inception to the end of 2011 were available for analysis (145). In a recent analysis of the NCDR ICD Registry, 22.5% of patients received a nonevidence-based ICD implantation, many identified by clinical situations addressed in this document: 8.3% of patients received an ICD within 40 days of an MI, 0.7% within 3 months of a CABG, and 14.0% within 3 months of an initial heart failure diagnosis (146). Another analysis of the ICD registry found that the magnitude of survival benefits described in randomized controlled trials was similar to the survival benefits in a comparable patient group from the NCDR (147). In its latest iteration, the NCDR-ICD Registry has been collecting data on ICD replacements and lead longevity. Although the accuracy of some components of the registry data has been questioned, the final solution must be for hospitals and health care providers to make accurate documentation and data input a high priority. Although the NCDR is publicly funded, industry and other groups

also maintain a number of registries on ICD use. Additional registries can provide "cross-checking" of the NCDR, and those registries that are maintained by industry must be made as transparent as possible with scientific access.

Part of improving registry data as the United States continues to slowly evolve to a fully electronic health record is the standardization of definitions for key data elements. Recently, the 2013 ACC/AHA Key Data Elements and Definition for Measuring the Clinical Management and Outcomes of Patients with Acute Coronary Syndromes and Coronary Artery Disease has been published (148). This document will help improve consistency and overall quality among hospitals and health care providers. Initiatives that standardize data elements and define best practice relating to ICD therapy will be critical for leveraging the benefits of ICD therapy to large populations.

Although recent medical literature and popular press have focused on inappropriate use of ICDs, it is also important to acknowledge that there are patients who would benefit from ICD therapy who do not receive counseling on the potential benefits of this therapy. Castellanos et al. (149) mailed a survey about the ICD guidelines to 3,000 physicians, composed of equal numbers of family practice physicians, internists, and general cardiologists selected randomly from the American Medical Association Masterfile. Answers discordant with the current guidelines were extremely common. In fact, almost 30% of respondents, including 7% of cardiologists, would never refer patients for consideration of a primary prevention ICD. In another analysis, investigators examined the Improve the Use of Evidence Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) database, and found that of 7,221 patients who met Class I criteria for ICD patients (after excluding 4% of patients who had documented contraindications), 3659 patients (50.7%) received ICDs (150). In addition, when examining individual practices, the use of ICDs in eligible patients ranged from 0%-100%, with the 10th and 90th percentiles 27.3% and 74.6%, respectively. Subsequent analysis of the IMPROVE database after the institution of quality improvement measures demonstrated a significant increase in guideline adherence (absolute improvement of 18%) from baseline to 24 months (151).

Future research should continue to evaluate the effectiveness and value of ICD therapy. For determining value, lifetime costs and benefits must be calculated. Although the first iteration of the NCDR focused on immediate postprocedural complications, the most recent version of the registry incorporates longitudinal follow-up. This transition is important because ICD therapy must be evaluated in its entirety. Complications with device replacements and appropriate and individualized programming of ICDs have important effects on the overall costs. Another important downstream complication is lead fracture or device malfunction. Over the past decade, there have been several highly publicized recalls of ICD generators and leads. Historically, the annual failure rate for ICD leads has been <1% per year, but two smaller-caliber leads—the Medtronic Sprint Fidelis and the St. Jude Riata leads—have higher annual failure rates, approaching 5% per year (152). When evaluating the value of ICD therapy, both additional costs and benefits must be taken into account.

Finally, it is critical that there is consistency among the various documents that clinicians use to guide therapy choices and that guide reimbursement. As mentioned earlier, there are several guideline documents that provide basic recommendations for ICD use that are based on strong evidence from randomized clinical trials. Documents such as this consensus statement and the 2013 Appropriate Use Criteria for ICDs attempt to assist the physician in caring for a patient with unique clinical characteristics (9). As addressed in this document, differences in interpretation of the clinical data can lead to different recommendations, which might be unavoidable given the complexities of clinical medicine and differences in the interpretation of data. However, it is critical for the writing committees of these documents to carefully assess the consistency of new documents and acknowledge and discuss differences. Reimbursement tables for medical care, such as National Coverage Determination statements produced by the United States Federal Government, are often not updated as frequently as clinical documents. For example, the National Coverage Determination for ICD therapy was last updated in 2005. Since this publication, there have been three Guidelines, two Focused Updates of previously published Guidelines, one Appropriate Use Document, and now two consensus statements relevant to ICD implantation that would be applicable to patients in the United States.

Since its inception more than 40 years ago, the ICD has evolved to a widely accepted and important treatment for patients with cardiovascular disease who are at risk of life-threatening ventricular arrhythmias. As with any complex and expensive treatment, we must continue to refine our understanding of who benefits from ICD implantation and how to optimally implement ICD therapy in these patients.

APPENDIX A

See **Table A1** for Writing Group disclosures and **Table A2** for Peer Reviewer disclosures.

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TABLE A1 Writing Group Disclosure Table

Writing Group	Employment	Consultant/ Advisory Board	Speakers' Bureau/ Honoraria	Research Grant	Fellowship Support	Board Mbs/ Stock Options/ Partner	Others
Hugh Calkins, MD, FHRS, CCDS	Johns Hopkins Hospital	None	None	4: Medtronic, Inc., St. Jude Medical	None	None	None
Fred M. Kusumoto, MD, FHRS	Mayo Clinic	None	None	None	None	None	None
David J. Slotwiner, MD	Hofstra North Shore – Long Island Jewish School of Medicine	None	None	None	None	None	None
Michael R. Gold, MD, PhD, FHRS	Medical University of South Carolina	1: Biotronik, St. Jude Medical, Sorin Group, Thoratec Corporation 2: Boston Scientific Corp. 3: Medtronic, Inc.	None	2: Medtronic, Inc., St. Jude Medical, Boston Scientific Corp.	3: Medtronic, Inc.	None	None
Alfred E. Buxton, MD	Beth Israel Deaconess Medical Center	1: Boston Scientific Corp., Forest Pharmaceuticals, Medtronic, Inc., St. Jude Medical	None	1: Medtronic, Inc.	1: Medtronic, Inc., Biosense Webster, Inc.	None	None
Stefan H. Hohnloser, MD, FHRS	J.W. Goethe University, Department of Medicine, Division of Cardiology	1: Boehringer Ingelheim, Bayer HealthCare, LLC, Bristol-Myers Squibb, St. Jude Medical, Johnson & Johnson 2: Sanofi Aventis	1: Sanofi Aventis, Boehringer Ingelheim, Bayer HealthCare, LLC, Bristol-Myers Squibb, St. Jude Medical, Minnesota Partnership for Biotechnology and Medical Genomics/University of Minnesota	None	None	None	None
Julia Indik, MD, PhD, FHRS	University of Arizona, Sarver Heart Center	None	None	None	None	None	None
Mina K. Chung, MD, FHRS	Cleveland Clinic, Department of Cardiovascular Medicine	0: Boston Scientific Corp., Medtronic, Inc., Biotronik, St. Jude Medical, Zoll Medical Corporation, Amarin 1: National Institutes of Health	1: American College of Cardiology Foundation	5: National Institutes of Health	None	None	Royalty Income; 1: Jones & Bartlett Publishers, Up to Date
Paul D. Varosy, MD, FHRS	VA Eastern Colorado Health Care System, Cardiology	None	None	None	None	None	None
Mandeep R. Mehra, MD	Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School	1: Boston Scientific, St. Jude Medical, Medtronic, Inc., Abbott Vascular, Johnson & Johnson, National Heart, Lung, and Blood Institute, Thoratec, American Board of Internal Medicine	None	None	None	None	5: Editor, ISHLT

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TABLE A1 Continued

Writing Group	Employment	Consultant/ Advisory Board	Speakers' Bureau/ Honoraria	Research Grant	Fellowship Support	Board Mbs/ Stock Options/ Partner	Others
Lisa Welikovitch, MD	Department of Cardiac Services, University of Calgary	None	None	None	None	None	None
Win-Kuang Shen, MD	Mayo Clinic College of Medicine	None	None	None	None	None	None
John Boehmer, MD	Penn State Hershey Medical Center	1: Medtronic, Inc., St. Jude Medical 2: Boston Scientific Corp.	None	2: St. Jude Medical	None	None	None
Richard Lee, MD, MBA	St. Louis University	None	None	None	None	None	None
Richard L. Page, MD, FHRS	University of Wisconsin School of Medicine and Public Health	None	None	None	None	None	None
Lynne Warner Stevenson, MD	Brigham & Women's Hospital	None	None	None	None	None	None
Venu Menon, MD	Cleveland Clinic	None	None	None	None	None	None

0 = $0; 1 = <$10,000; 2 = >$10,001 to <$25,000; 3 = >$25,001 to <$50,000; 4 = >$50,001 to <$100,000; 5 = >$100,001.

TABLE A2 Peer Reviewer Disclosure Table

Peer Reviewer	Consultant/Advisory Board	Speakers' Bureau/ Honoraria	Research Grant	Fellowship Support	Board Mbs/ Stock Options/ Partner	Others
Sharon Hunt, MD	None	None	None	None	None	None
John Burnett, MD	2: Chaire, Nile Therapeutics, Trevena, Bayer, Novartis, Merck, Anexon	None	None	None	1: Zumbro Discovery	1: Intellectual property rights, Nile Therapeutics
James R. Edgerton, MD	3: AtriCure	3: AtriCure	None	None	None	None
Sana Al-Khatib, MD	None	None	None	None	None	None
Anne Curtis, MD	1: Bristol-Myers Squibb, Janssen Pharmaceuticals, Biosense Webster, Inc., Sanofi Aventis, St. Jude Medical, Daiichi Sankyo, Pfizer, Jones & Bartlett	None	2: Medtronic, Inc.	None	None	None
Valentin Fuster, MD, PhD	None	None	None	None	None	None
David R. Holmes, Jr., MD	None	None	None	None	None	None
Jodie L. Hurwitz, MD	1: Biosense Webster, Inc.	1: St. Jude Medical, Medtronic Inc., Boehringer Ingelheim	None	None	None	0: Heart Rhythm Society 1: The Heart Hospital Baylor Plan, Medical City Hospital
Gregory M. Marcus, MD	None	None	3: Medtronic, Inc., Gilead 5: SentreHeart	None	None	None

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TABLE A2 Continued

Peer Reviewer	Consultant/Advisory Board	Speakers' Bureau/ Honoraria	Research Grant	Fellowship Support	Board Mbs/ Stock Options/ Partner	Others
Simone Musco, MD	None	1: Bristol-Myers Squibb, Pfizer	None	None	None	None
Patrick T. O'Gara, MD	None	None	None	None	None	1: Lantheus Medical Imaging 2: National Institutes of Health
Brian Olshansky, MD	1: Boston Scientific Corp., Boehringer Ingelheim, Medtronic, Inc., Bio-Control Medical, Ltd., Sanofi Aventis, Amarin	None	None	None	None	1: Sanofi Aventis, Boston Scientific, Amarin
Marwan Refaat, MD	None	None	None	None	None	None
Frederico Gentile, MD	None	None	None	None	None	None
L. Samuel Wann, MD	1: United Healthcare	None	None	None	None	None

0 = $0; 1 = <$10,000; 2 = >$10,001 to <$25,000; 3 = >$25,001 to <$50,000; 4 = >$50,001 to <$100,000; 5 = >$100,001.