Implantable Cardioverter Defibrillator

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Next Review: April 2022
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DESCRIPTION

The automatic implantable cardioverter defibrillator (ICD) is a device designed to monitor a patient's heart rate, recognize ventricular fibrillation (VF) or ventricular tachycardia (VT), and deliver an electric shock to terminate these arrhythmias to reduce the risk of sudden cardiac death. Indications for ICD implantation can be broadly subdivided into 1) primary prevention, i.e., their use in patients who are considered at high risk for sudden cardiac death but who have not yet experienced life-threatening VT or VF; and 2) secondary prevention, i.e., their use in patients who have experienced a potentially life-threatening episode of VT (near sudden cardiac death).

MEDICAL POLICY CRITERIA

I. Transvenous or subcutaneous implantable cardioverter defibrillator (ICD) implantation in pediatric patients (less than 18 years of age) may be considered **medically necessary**.

II. The use of a _transvenous_ automatic implantable cardioverter defibrillator (ICD) may be considered **medically necessary** in adult patients (age 18 and older) who are not candidates for a cardiac revascularization procedure (coronary artery bypass graft

[CABG] or percutaneous transluminal coronary angioplasty [PTCA]) and who meet one of the following criteria (A. or B.):

A. For *primary* prevention when one or more of the following criteria are met:

1. Ischemic cardiomyopathy with New York Heart Association (NYHA) functional Class I symptoms (See Policy Guidelines) when both of the following criteria (a. and b.) are met:

   a. History of myocardial infarction at least 40 days before ICD treatment; and

   b. Left ventricular ejection fraction of 30% or less.

2. Ischemic cardiomyopathy with NYHA functional Class II or Class III symptoms (See Policy Guidelines) when both of the following criteria (a. and b.) are met:

   a. History of myocardial infarction at least 40 days before ICD treatment; and

   b. Left ventricular ejection fraction of 35% or less.

3. Nonischemic cardiomyopathy, including arrhythmogenic right ventricular cardiomyopathy, or neuromuscular disorders when one or more of the following criteria are met:

   a. Syncope presumed due to ventricular arrhythmia; or

   b. All of the following criteria are met:

      i. Left ventricular ejection fraction of 35% or less; and

      ii. Reversible causes have been excluded; and

      iii. Response to optimal medical therapy has been adequately determined.

4. Heart failure with left ventricular ejection fraction of 40% or less, who are awaiting heart transplantation and will be discharged home

5. Nonhospitalized heart failure patients with NYHA Class IV symptoms (see Policy Guidelines) that are candidates for a left ventricular assist device (LVAD) or cardiac transplantation

6. Hypertrophic cardiomyopathy (HCM) at high risk for sudden cardiac death with at least one of the following major risk factors:

   a. History of premature HCM-related sudden death in one or more first-degree relatives younger than 50 years; or

   b. Left ventricular hypertrophy greater than 30 mm; or

   c. One or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; or

   d. Prior unexplained syncope inconsistent with neurocardiogenic origin

   e. Abnormal blood pressure response to exercise.

7. Documented *LMNA* gene mutations (lamin A/C deficiency) in patients with at least one of the following conditions:

      a. Cardiomyopathy; or

      b. Symptomatic cardiac arrhythmias; or

      c. Left ventricular ejection fraction less than 45%; or

      d. Nonsustained ventricular tachycardia; or

      e. Nonsense *LMNA* variant.

8. Diagnosis of long QT syndrome (LQTS) with at least one of the following:

      a. Prior cardiac arrest; or

      b. Recurrent syncopal events while on beta blocker therapy.

9. Diagnosis of Brugada syndrome (BrS) with at least one of the following:

      a. Prior cardiac arrest; or

      b. Spontaneous sustained ventricular tachycardia (VT) with or without syncope; or

      c. Spontaneous diagnostic type 1 ECG with a history of syncope, seizure, or nocturnal agonal respiration after noncardiac causes have been excluded; or

      d. Development of ventricular fibrillation (VF) during programmed electrical stimulation.

10. Diagnosis of catecholaminergic polymorphic ventricular tachycardia (CPVT) with at least one of the following:

      a. Prior cardiac arrest; or

      b. Recurrent syncope; or

      c. Polymorphic/bidirectional VT that is nonresponsive to medical management, or left cardiac sympathetic denervation.

11. Diagnosis of short QT syndrome (SQTS) with at least one of the following:

      a. Prior cardiac arrest; or

      b. Symptomatic and have documented spontaneous VT with or without syncope; or

      c. Family history of sudden cardiac death.

12. Diagnosis of cardiac sarcoidosis with at least one of the following:

      a. Prior cardiac arrest; or

      b. Sustained VT; or

      c. Left ventricular ejection fraction of 35% or less.

13. Diagnosis of adult congenital heart disease with hemodynamically unstable VT or VF.

14. Patients with a left ventricular assist device (LVAD) and sustained ventricular arrhythmia

B. For *secondary* prevention in patients who meet one or more of the following:

1. History of a life-threatening clinical event associated with ventricular arrhythmic events such as sustained ventricular tachyarrhythmia, after reversible causes (e.g., acute ischemia) have been excluded; or

2. Diagnosis of nonischemic cardiomyopathy or ischemic heart diseases with at least one of the following:

    a. Hemodynamically unstable ventricular tachycardia; or

    b. Stable ventricular tachycardia not due to reversible causes (e.g., acute ischemia).

III. The use of the _transvenous_ ICD is considered **investigational** for adult patients when Criterion II. is not met and including, but not limited to, patients with one or more of the following:

   A. Have had an acute myocardial infarction (i.e., less than 40 days before ICD treatment); or

   B. Have New York Heart Association (NYHA) Class IV (See Policy Guidelines) congestive heart failure (unless patient is eligible to receive a combination cardiac resynchronization therapy ICD device); or

   C. Have had a cardiac revascularization procedure in the past 3 months (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]) or are candidates for a cardiac revascularization procedure; or

   D. Have noncardiac disease that would be associated with life expectancy less than one year.

IV. The use of the _subcutaneous_ ICD may be considered **medically necessary** in adult patients (age 18 years and older) who meet all of the following criteria (A.-C.):

   A. Applicable medical necessity criteria for _transvenous_ ICD is met (Criterion II.); and

   B. Have no indication for antibradycardia pacing; and

   C. Do not have ventricular arrhythmias that are known or anticipated to respond to antitachycardia pacing.

V. The use of the _subcutaneous_ ICD is considered **investigational** for adult patients when Criteria IV. are not met.

VI. Revision(s) or replacement(s) of a transvenous or subcutaneous ICD may be considered **medically necessary** after the device has been placed.

VII. The use of ICDs with an ST-segment monitoring feature in patients is considered **investigational** for all indications.

VIII. The use of extravascular (substernal lead) ICDs is considered **investigational** for all indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

New York Heart Association Classes

- NYHA Class I = No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).
- NYHA Class II = Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
- NYHA Class III = Marked limitation of physical activity; less than ordinary activity leads to symptoms
- NYHA Class IV = Inability to carry on any activity without symptoms; symptoms may be present at rest

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical/Chart Notes
- Documentation of symptoms, associated diagnoses and treatments
- Type of ICD being requested

CROSS REFERENCES

1. Intracardiac Ischemia Monitoring, Surgery, Policy No. 208
2. Leadless Cardiac Pacemakers, Surgery, Policy No. 217

BACKGROUND

The standard ICD involves placement of a generator in the subcutaneous tissue of the chest wall. Transvenous leads are attached to the generator and threaded intravenously into the endocardium. The leads sense and transmit information on cardiac rhythm to the generator which analyzes the rhythm information and produces an electrical shock when a malignant arrhythmia is recognized.

A totally subcutaneous ICD (S-ICD®) has also been developed. This device does not employ transvenous leads, and thus avoids the need for venous access and complications associated with the venous leads. Rather, a subcutaneous electrode is implanted adjacent to the left sternum. The electrodes sense the cardiac rhythm and deliver countershocks through the subcutaneous tissue of the chest wall.

ICDs with a built-in ST-segment monitoring feature, also called ICD-based ischemia monitors, are currently being studied. ST segment monitoring may also be referred to as intracardiac ischemia monitoring. The continuous ST-segment monitoring provided by this added feature is intended to detect changes in the patient's ST-segment as a possible indicator of an ischemic cardiac event. If an ST segment shift meets or exceeds a preprogrammed threshold, the device stores the event data (e.g., date, time, heart rate, maximum ST shift, duration of the event). The device has a patient notifier feature that vibrates to alert the patient that an ST episode has occurred.

Extravascular (EV) ICDs have been developed, which have lead placement under the sternum. These devices are designed to provide the benefits of transvenous ICDs while avoiding the complications associated with intravascular lead placement.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has approved a number of ICDs through the premarket approval (PMA) process. The FDA-labeled indications generally include patients who have experienced life-threatening ventricular tachyarrhythmia associated with cardiac arrest or ventricular tachyarrhythmia associated with hemodynamic compromise and resistance to pharmacologic treatment.

The following are examples of FDA-approved transvenous ICDs:

- Devices manufactured by Boston Scientific include Dynagen, Inogen, Origen, and Teligen.
- Medtronic produces the Evera Family of devices (originally: Virtuosos/Entrust/Maximo/Intrinsic/Marquis family).
- St. Jude Medical, Inc. devices include the Ellipse / Fortify Assura Family and the Current Plus ICD (originally: Cadence Tiered Therapy Defibrillation System).
- Other devices with similar approval language include devices from Biotronik, Boston Scientific, and Sorin CRM USA.

The following are examples of FDA-approved subcutaneous ICDs:

- The Subcutaneous Implantable Defibrillator (S-ICD®) System (Cameron Health, Inc., acquired by Boston Scientific, Inc.) received FDA approval on September 28, 2012 for "defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous frequently recurring ventricular tachycardia that is reliably terminated with antitachycardia pacing." The electrode is called the Q-TRAK® and the electrode insertion tool is called the Q-Guide™.
- The Emblem S-ICD™ (Boston Scientific, Inc.), which is smaller and longer-lasting than the original S-ICD, was cleared for marketing through a PMA supplement.

Currently, there are no FDA-approved EV ICDs.

Note: This policy addresses only initial ICD implantation; it does not address ICD removal or replacement.

EVIDENCE SUMMARY

TRANSVENOUS IMPLANTABLE CARDIAC DEFIBRILLATOR (ICD)

The scientific evidence evaluating the use of automatic ICDs on health outcomes consists of several technology assessments and clinical trials. Evidence from well-conducted randomized controlled trials (RCTs) shows consistent associations between use of ICDs and improved health outcomes among specific groups of patients with symptomatic ischemic or nonischemic dilated cardiomyopathy and those with history of prior arrhythmogenic events.

ICDS FOR HEART FAILURE AND CARDIOMYOPATHY

Systematic Reviews

In 2016, results from the Danish Study were published. This was a multi-center RCT comparing ICD to standard management in patients with non-ischemic heart failure, described in more detail below.[1] While the trial demonstrated a significantly lower risk of sudden cardiac

death (SCD) with ICD, there was no difference seen in overall mortality. After this article was published, several systematic reviews evaluated the evidence from RCTs on ICD use in patients with nonischemic cardiomyopathy.

A 2018 Cochrane review included six RCTs (n=3,128) and reported that ICD use plus optimal medical therapy had a survival benefit compared with optimal medical therapy alone (hazard ratio [HR] 0.78, 95% confidence interval [CI] 0.66 to 0.92), but the authors noted that ICD use likely increases the risk of adverse events.[2] Wolff (2015) meta-analyzed five RCTs, with a total of 2,992 dilated cardiomyopathy patients, that compared ICD therapy with medical therapy for primary prevention.[3] They found a significant reduction in mortality and sudden cardiac death with ICD therapy (odds ratio [OR] 0.77, 95% CI 0.64 to 0.93, p=0.006 and OR 0.43, 95% CI 0.27 to 0.69, p = 0.0004, respectively).

Similarly, Luni (2017) performed a meta-analysis of six RCTs evaluating ICD use for primary prevention in patients with nonischemic cardiomyopathy.[4] While they reported a significant survival benefit with ICD therapy, this benefit was no longer significant when the analysis was restricted to trials which had adequate beta blocker, ACE/ARB and aldosterone receptor blocker use. A meta-analysis by Al-Khatib (2017) included only four RCTs, as they included only trials that compared ICD to medical therapy that had at least 100 nonischemic cardiomyopathy patients and follow-up periods of at least 12 months.[5] This analysis also reported a significant mortality reduction with ICD therapy (HR 0.75, 95% CI 0.61-0.93, p=0.008). A meta-analysis by Siddiqui (2018), which included six RCTs, similarly reported a lower mortality rate with ICD compared to medical therapy (OR 0.74, 95% CI 0.62 to 0.90, p=0.002), and compared to amiodarone treatment (OR 0.66, 95% CI 0.44 to 0.98, p=0.04).[6] Other meta-analyses have shown similar results.[7, 8]

Gracieux (2014) published the results of a systematic review of nine RCTs of adults aged 19 years or older with ischemic cardiomyopathy to determine the incidence and predictors of appropriate ICD therapy delivery.[9] Only four of the nine RCTs that met inclusion criteria reported the clinical characteristics of patients who received appropriate shocks. These characteristics included male sex, advanced NYHA class, nonsustained ventricular tachycardia, and lower serum creatinine. These patients were also less likely to be on beta-blocker medications. LVEF was not a significant factor. The authors noted that predictors of appropriate shocks were not adequately studied in large trials and recommended further large prospective studies.

A 2013 technology assessment from the Agency for Healthcare Research and Quality (AHRQ) assessed the evidence published through December 4, 2012 for ICDs for primary prevention of sudden cardiac death.[10] Included studies were RCTs or comparative cohort studies comparing ICD to no ICD or to different ICD interventions, a minimum of 10 participants per study group, and concurrent controls in the cohort studies. Patients in the ICD groups must have been followed from the time of ICD implantation. Key questions were well defined and focused on the following:

- Outcomes of 1) ICD vs. no ICD, 2) ICD with antitachycardia pacing (ATP) vs. ICD alone, and 3) ICD with cardiac resynchronization therapy (CRT) vs. ICD alone
- Variations in outcomes and adverse events among subgroups of participants, ICD devices, clinicians, and facilities
- Eligibility criteria and methods for evaluation of participants in comparative trials

- Likelihood of SCD or ventricular tachyarrhythmia (VT) as measured by total shocks in patients with ICDs or SCD episodes in patients without ICDs.

Ten RCTs (18 articles[11-27]) and four cohort studies[28-31] of adults met inclusion criteria.; no studies of ICDs in children met inclusion criteria. All included studies conducted intention-to-treat analyses. In studies comparing ICD to no ICD the strength of evidence for all-cause mortality and SCD was rated as high. These studies found reduced risk of all-cause mortality three to seven years after ICD implantation and SCD two to six years after implantation (HR 0.69 and 0.37, respectively). There was indirect evidence across studies that ICD provided no benefit for patients with recent myocardial infarction (MI), defined as <30-40 days. No significant difference was found for all-cause mortality or SCD across subgroups by patient sex or age or by the facilities in which the ICDs were placed. The evidence for quality of life in these studies was rated as low and failed to show consistent effects of ICD placement. No studies reported the effect of adding ATP in ICD patients. Four RCTs[32-35] that compared ICD alone to ICD with CRT (CRT-D) met inclusion criteria, but the strength of evidence was rated as insufficient due to discordant findings.

Eligibility criteria for ICD implantation in 13 of the 14 studies included both ischemic or nonischemic dilated cardiomyopathy (DCM) and left ventricular ejection fraction (LVEF) $\leq$35%. Most of the studies excluded adults over 70 to 80 years of age. Heart failure (HF) class varied between studies. While most RCTs tested ICD patients for nonsustained VT, different diagnostic tools were used. Only one RCT used electrophysiology studies (EPS) in all participants. Coronary angiography or exercise testing for coronary stenosis was tested in four of the RCTs. Limitations of the included studies were high attrition rates (>20%), differential attrition and/or crossover rates between study groups, and between-group differences in concurrent beta blocker use and control treatments. In addition, outcome assessors were not blinded. The authors concluded that there was high strength evidence in favor of ICD therapy compared to no ICD therapy for primary prevention of SCD in certain patients with reduced LVEF and ischemic or non-ischemic cardiomyopathy (NICM).

Chen (2013) analyzed eight RCTs[32, 36-54] that compared the safety and effectiveness of ICD alone with cardiac resynchronization therapy and ICD (CRT-D) in patients with heart failure.[55] The study quality was rate as high in four RCTs with follow-up of more than six months. The quality of the other four RCTs was down-graded slightly due to short-term follow-up of less than six months. CRT-D showed significantly superior outcomes compared to ICD alone for cardiac function, improved clinical condition, fewer hospitalizations, and lower all-cause mortality 12 months or more after implantation, though not during the initial three to six months after implantation. However, CRT-D had a significantly higher rate of serious adverse events (e.g., pneumothorax, hemothorax, lead dislodgement, coronary sinus dissection). There were a number of methodological limitations of the meta-analysis and the included RCTs. The limitations included the between-study differences in follow-up duration noted above. In addition, some studies included primarily NYHA class I and II heart failure patients while others focused on class III and IV patients. The authors also noted that the enrolled patients were younger than the general population of candidates for ICD or CRT-D which could result in an overestimation of benefit since older patients would be expected to have more comorbidities that could negatively impact clinical outcomes.

Shinkel (2012) reported the results of a systematic review and meta-analysis of 16 studies[56-58] of patients with ICDs for hypertrophic cardiomyopathy (HCM).[59] Mean age was 42 years and mean follow-up was 3.7 years. The majority of the studies were for primary prevention ICDs.

Risk factors for SCD included left ventricular wall thickness $\geq$30 mm, family history of SCD, nonsustained ventricular tachycardia, syncope, and abnormal blood pressure response. The rate of appropriate ICD therapy was 14%, with annualized rate of 3.3%. Inappropriate shocks occurred in 20% of the 1966 patients in the 13 studies that reported this outcome. The annualized rate of inappropriate therapy was 4.8%. Mortality rates were reported in 13 studies and included 3% from cardiac death and 2% from noncardiac death. Nine studies reported adverse events which occurred in 15% of patients. The most frequent complications were lead malfunction (7%) or displacement (3%) and infection (3%). Limitations of the meta-analysis included the use of data from observational studies, and the potential risk of heterogeneity of participant clinical characteristics and SCD risk profiles when pooling data from different studies. Limitations of the included studies were the lack of clear information on the clinical decision strategy and risk factors for ICD placement, lack of long-term data on ICD-related complications in the general practice setting, younger age of participants than would be expected in the general clinical setting, and insufficient consideration of the psychological and behavioral aspects of ICD therapy in HCM patients. This latter limitation is important because many HCM patients who are candidates for ICD are otherwise healthy, asymptomatic young individuals.

Randomized Controlled Trials (RCTs)

A study by Biton (2018) evaluated the impact NYHA class on long-term survival with ICD therapy in patients from the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II).[60] There were 1,164 patients in the study, 442 were NYHA I, 425 were NYHA II, and 297 were NYHA III. All had a documented prior MI. After eight years of follow-up, mortality was lower for the ICD treatment group compared with non-ICD therapy, regardless of HF symptoms (NYHA I HR 0.63, 95% CI 0.46 to 0.85, p=0.003; NYHA II HR 0.68, 95% CI 0.50 to 0.93, p=0.017; NYHA III HR 0.68, 95% CI 0.50 to 0.94, p=0.018).

Kober (2013) reported results from the Danish Study in 2016,[1] which was included in several of the recent systematic reviews described above. This unblinded trial included 556 patients with NICM, enrolled between 2008 and 2014 from multiple centers in Denmark, to compare ICD therapy to usual clinical care. As many patients with heart failure are not treated with CRT, the randomization of patients was stratified such that both ICD and control groups had a similar proportion of CRT patients (58%). The primary outcome of the study was death from any cause, and secondary outcomes included sudden cardiac death, cardiovascular death and non-fatal MIs. The median follow-up time was 67.6 months (interquartile range, 49-85 months). There were 120 patients (21.6%) in the ICD group and 131 patients in the control group that died during follow-up (4.4 and 5.0 deaths/100 person-years, respectively), which was not significantly different. Subgroup analysis showed no difference in ICD effect between patients receiving CRT and those who did not, but younger patients (< age 59) did demonstrate a survival benefit with ICD (HR 0.51, 95% CI 0.29 to 0.92). The risk for cardiovascular death was also not significantly different between groups (HR for ICD group vs. control, 0.77, 95% CI 0.57 to 1.05, p=0.10). However, sudden cardiac death was far less frequent in the ICD group than in controls (HR 0.50, 95% CI 0.31 to 0.82). The lack of benefit with IDC therapy for overall survival seen in this study differs from previous findings. The authors concluded that recent advances in heart failure treatment, including CRT, have reduced the potential benefit from ICD therapy, except in select patients.

Non-randomized Studies

Ischemic or Dilated Cardiomyopathy

Zabel (2020) published results of the EUropean Comparative Effectiveness Research to Assess the Use of Primary ProphylacTic Implantable Cardioverter-Defibrillators (EU-CERT-ICD) study, a multicenter controlled cohort study evaluating ICD use for primary prevention in patients with ischemic or dilated cardiomyopathy.[61] Of the 2,327 patients that were recruited for the study, 2,247 had sufficient data for analysis: 1,516 who had ICD implantation and 731 controls who did not have ICD implantation. After a mean follow-up of 2.4 years, mortality was significantly lower in the ICD group after adjustment for other mortality predictors, such as age and LVEF (HR 0.731, 95% CI 0.569 to 0.938, p=0.014). ICDs did not appear to benefit patients with diabetes or those above age 75.

Nonischemic Cardiomyopathy

A multi-center study using data from the German Device Registry was published by Frommeyer (2019).[62] This registry includes 5,451 patients with one year of follow-up who had a device implanted. Of these, 779 were patients with NICM and a LVEF of 35% or less. Among these 779 patients, 56% received a cardiac resynchronization therapy defibrillator system, 33% received a single-chamber ICD, and 11% received a dual-chamber ICD. After a median follow-up of 16.1 months, 9.3% of the patients had died. Mortality was significantly higher in patients aged 68 years and above (7.9%) compared with patients aged 59 to 68 years (2.5%) or below age 59 (3.8%, p<0.015).

Amara (2017) compared ICD therapy for the prevention of sudden cardiac death in patients with NICM and ischemic cardiomyopathy (ICM) enrolled in the multicenter Défibrillateur Automatique Implantable-Prévention Primaire (DAI-PP) study.[63] A total of 5,485 patients participated in the study: 2,181 (39.8%) with NICM and 3,304 (60.2%) with ICM. The mean follow-up was 3.1 ± 2.2 years. Patients with ICM were significantly older (63.7 ±10.3 vs. 60.6 ± 12.2 years, p<0.0001) and had a higher prevalence of sinus rhythm (77.3% vs. 74.0%, p=0.009), a higher ejection fraction (27% vs. 25%, p<0.0001), and a narrower QRS (37.3% vs. 21.4% with QRS <120, p<0.0001) than those with NICM. Mortality during follow-up was significantly higher in ICM patients, at 52.3 events/1000 person-years vs. 48.6 events/1000 person-years for NICM patients (p=0.008). This difference was primarily due to increased non-cardiovascular mortality, as cardiovascular mortality rates were similar between groups. The authors noted that inappropriate therapies were more frequent in those with NICM (7.94 vs. 5.96%, p=0.005).

Results from subjects with nonischemic dilated cardiomyopathy (NIDCM) included in SCD-HeFT and DEFINITE studies suggested a mortality benefit from ICD therapy, although statistical significance that was not achieved in these studies was likely related to insufficient power.

Hypertrophic Cardiomyopathy

Magnusson (2015) reported outcomes for 321 patients with HCM treated with an ICD enrolled in a Swedish registry.[64] Over a mean 5.4 years of follow-up, appropriate ICD discharges in response to ventricular tachycardia or fibrillation occurred in 77 patients (24%), corresponding to an annual rate of appropriate discharges of 5.3%. At least one inappropriate shock occurred in 46 patients (14.3%), corresponding to an annualized event rate of 3.0%. Ninety-two patients (28.7%) required at least one surgical intervention for an ICD-related complication, with a total

of 150 ICD-related reinterventions. Most reinterventions (n=105, 70%) were related to lead dysfunction.

ICDS IN PATIENTS WITH *LMNA* GENE MUTATION

In a systematic review for GeneReviews®, Hershberger (2016) concluded, "Because risk for sudden cardiac death in *LMNA*-related DCM accompanies heart block and bradyarrhythmias, ICD use (rather than just pacemaker use) has been recommended for all indications."[65]

Pasotti (2008) conducted a retrospective longitudinal study with 94 individuals with mutations in the *LMNA* gene.[66] Subjects were observed for a median follow-up time of 57 months. During follow-up, 20 patients received a pacemaker and 16 received an ICD implantation. Twelve appropriate ICD interventions detected by the device (eight ventricular fibrillation and four sustained VT). None of the subjects with ICDs died from sudden cardiac death, whereas the pacemaker did not appear to protect from SCD.

ICDS IN PATIENTS WITH CARDIAC ION CHANNELOPATHIES

ICDs have been used for both primary and secondary prevention in patients with a number of disorders that predispose to ventricular arrhythmias and sudden cardiac death, including long QT syndrome (LQTS), Brugada syndrome (BrS), short QT syndrome (SQTS), and catecholaminergic polymorphic ventricular tachycardia (CPVT). Some of these conditions are extremely rare, but the use of ICDs has been described in small cohorts of patients with BrS, LQTS, and SQTS. These small cohort studies are listed below:

Long QT Syndrome

Horner (2010) reported on outcomes for 51 patients with genetically confirmed LQTS treated with an ICD from 2000 to 2010 who were included in a single-center retrospective analysis of 459 patients with genetically confirmed LQTS.[67] Of the patients treated with ICDs, 43 (84%) received the device as primary prevention. Twelve patients (24%) received appropriate ventricular fibrillation or torsades de pointes- terminated ICD shocks. Factors associated with appropriate shocks included secondary prevention indications (p=0.008), QT corrected (QTc) duration greater than 500 ms (p=0.0008), non-LQT3 genotype (p=0.02), documented syncope (p=0.05), documented torsades de pointes (p=0.003), and a negative sudden family death history (p=0.0001). Inappropriate shocks were delivered in 15 patients (29%). Patients with the LQT3 genotype had only received inappropriate shocks.

Brugada Syndrome

A systematic review by Kusumoto (2018) compared ICD outcomes for asymptomatic Brugada syndrome (BrS) patients with and without inducible ventricular arrhythmia on electrophysiology study.[68] A meta-analysis of five studies reported OR of 2.3 (95% CI 063 to 8.66, p=0.2) for major arrhythmic events in those with inducible ventricular arrhythmia compared to those without. The authors noted that there was a low overall event rate in this asymptomatic population.

Hernandez-Ojeda (2017) reported on results from a single-center registry of 104 patients with BrS who were treated with ICDs. Ten (9.6%) patients received an ICD for secondary prevention and in 94 (90.4%) patients received an ICD for primary prevention. During the average 9.3-year follow-up, 21 (20.2%) patients received a total of 81 appropriate shocks. In multivariate analysis, type 1 electrocardiogram with syncope and secondary prevention

indication were significant predictors of appropriate therapy. Nine (8.7%) patients received 37 inappropriate shocks. Twenty-one (20.2%) patients had other ICD-related complications.

Conte (2015) described outcomes for a cohort of 176 patients with spontaneous or drug-induced Brugada type 1 electrocardiographic findings who received an ICD at a single institution and were followed for at least six months.[69] Before ICD implantation, 14.2% of subjects had a history of aborted SCD due to sustained spontaneous ventricular arrhythmias, 59.7% had at least one episode of syncope, and 25.1% were asymptomatic. Over a mean follow up of 83.8 months, 30 patients (17%) had spontaneous sustained ventricular arrhythmias detected. Sustained ventricular arrhythmias were terminated by ICD shocks or antitachycardia pacing in 28 patients (15.9%) and two patients (1.1%), respectively. However, 33 patients (18.7%) experienced inappropriate shocks. Eight patients (4.5%) died during follow up, three of whom died of cardiac causes.

Dores (2015) reported results of a Portuguese registry that included 55 patients with BrS, 36 of whom were treated with ICDs for either primary or secondary prevention.[70] Before ICD implantation, 52.8% of subjects were asymptomatic, 30.6% had a history of syncope with suspected arrhythmic cause, and 16.7% had a history of aborted SCD. Over a mean follow up of 74 months, seven patients experienced appropriate shocks, corresponding to an incidence of 19.4% and an annual event rate of 2.8%. In multivariate analysis, predictors of appropriate shocks were a history of aborted SCD (HR 7.87, 95% CI 1.27 to 49.6, p=0.027) and nonsustained ventricular tachycardia during follow up (HR 6.73, 95% CI 1.27 to 35.7, p=0.025).

In data from a US cohort of 33 patients with BrS treated with ICDs, Steven (2011) reported that two of three patients with a prior history of aborted SCD received appropriate shocks over a mean 7.9 years of follow up, while none of the 30 patients without a history of aborted SCD had an arrhythmia detected.[71] In a smaller registry that included 25 patients with BrS treated with ICDs, over an average follow up of 41.2 months, appropriate shocks were delivered in three patients, all of whom had prior cardiac arrest.[72]

Catecholaminergic Polymorphic Ventricular Tachycardia

A systematic review by Roston (2018) assessed the use of ICDs in patients with CPVT and included 53 studies (total n=1,429).[73] There were 503 patients that received an ICD in these studies, with 47.3% of the patients receiving the device for primary prevention. Only 12.8% were prescribed optimal antiarrhythmic therapy. More than 40% of the ICD patients had at least one appropriate shock during follow-up, while 20.8% had at least one inappropriate shock, 19.6% had electrical storm, and seven patients died (four due to an ICD-associated electrical storm). Other ICD complications were seen in 32.4% of the patients.

Roston (2015) published the results of a multicenter retrospective cohort study that included 226 patients with catecholaminergic polymorphic ventricular tachycardia.[74] Implantable cardioverter defibrillators were placed in 121 (54%) most often for history of cardiac arrest (67 patients [55%]). One or more treatment failure events while on beta blockers were documented in 42 patients (35%). Appropriate shocks were experienced by 56 patients (46%) and inappropriate shocks occurred in 21 patients (22%). Arrhythmia was terminated after appropriate shock in 31 patients (55%), but nine (16%) had poor response to appropriate shocks. Electrical storm occurred in 22 patients (18%). ICD-related complications occurred in 28 patients (23%), usually manifesting as lead problems in 16 (57%). There were no differences in number of appropriate shocks, success of shocks, or incidence of electrical storm between patients with and without history of cardiac arrest. Death occurred in three

patients (2%) despite ICD placement, one of which was associated with electrical storm. Fifty-eight patients (48%) were asymptomatic after ICD placement; however, 30 (25%) had persistent ventricular ectopy, 13 (11%) experienced syncope, and 13 (11%) had subsequent cardiac arrest.

Roses-Noguer (2014) reported results of a small retrospective study of 13 patients with CPVT who received an ICD.[75] The indication for ICD therapy was syncope despite maximal beta-blocker therapy in 6 patients (46%) and aborted SCD in seven patients (54%). Over a median follow-up of 4.0 years, 10 patients (77%) received a median four shocks. For 96 shocks, 87 electrocardiograms (ECGs) were available for review; of those, 63 (72%) were appropriate and 24 (28%) were inappropriate. Among appropriate shocks, 20 (32%) were effective in restoring sinus rhythm.

ICDS AND ADVERSE EVENTS

Ezzat (2015) published a systematic review and meta-analysis of adverse events (AEs) following ICD implantation, comparing rates of AEs reported in clinical trials of ICDs with those reported in the U.S. National Cardiovascular Data Registry.[76] The review included 18 RCTs with a total of 6,796 patients. In pooled analysis, the overall AE rate was 9.1% (95% CI 6.4 to 12.6%). Rates of access-related complications, lead-related complications, generator-related complications, and infection were 2.1% (95% CI 1.3 to 3.3%), 5.8% (95% CI 3.3 to 9.8%), 2.7% (95% CI 1.3 to 5.7%), and 1.5% (95% CI 0.8 to 2.6%), respectively. Complication rates in the RCTs were higher than those in the U.S. registry, which reports only in-hospital complications (9.1% in the RCTs vs. 3.08%, p<0.01). The overall complication rate was similar to that reported by Kirkfelt (2014) in a population-based cohort study including all Danish patients who underwent a cardiac implantable electronic device procedure from 2010 to 2011 (562/5918 patients [9.5%] with at least one complication).[77]

Persson (2014) published a systematic review and meta-analysis of AEs following ICD implantation.[78] The authors included data from 35 cohort studies, reported in 53 articles. In-hospital serious AE rates ranged from 1.2% to 1.4%, most frequently pneumothorax (0.4%-0.5%) and cardiac arrest (0.3%). Posthospitalization complication rates were variable: device-related complications occurred in 0.1% to 6.4%; lead-related complications in 0.1% to 3.9%; infection in 0.2% to 3.7%; thrombosis in 0.2% to 2.9%; and inappropriate shock in 3% to 21%.

The 2013 AHRQ technology assessment summarized above identified 14, 33, and 22 studies that reported early (up to 30 days after ICD implantation) AEs, late AEs, and inappropriate ICD shock, respectively.[10] The rate of early adverse events was 2.8% to 3.6% during hospitalization, of which 1.2% to 1.35% were considered serious events (strength of evidence high). The most common early AEs were lead dislodgement and hematoma. Higher early AE rates with found with dual chamber ICDs, in older patients, in women, and in patients with end-stage renal disease (ESRD). The most common late AEs were device-related AEs that occurred in <0.1% to 6.4% of ICD patients during follow-up ranging from 2 to 49 months (strength of evidence low). Lead malfunction, infection, and thrombosis were also reported. Inappropriate shocks at one to five years follow-up occurred in 3% to 21% of patients, with more occurring in younger patients. There was inconsistent evidence related to the rate of inappropriate shocks for single and dual chamber ICDs.

A systematic review and meta-analysis by Auricchio (2017) focused on inappropriate shocks from both single chamber ICDs (VR-ICDs) and subcutaneous ICDs (S-ICDs).[79] The review included 16 articles, which showed that an average of 6.4% (95% CI 5.1 to 7.9%) of patients

with these ICDs received an inappropriate shock per year. There was evidence that this proportion was lower in more recent studies and in studies with longer follow-up.

In contrast to patients requiring ICDs for secondary prevention or for primary prevention after acute MI, patients with hereditary arrhythmia syndromes are more likely to potentially require ICDs for primary prevention. Olde Nordkamp (2016) reported on a systematic review and meta-analysis of studies reporting on ICD complications in individuals with inherited arrhythmia syndromes.[80] The review included 63 cohort studies with a total of 4,916 patients (710 [10%] with arrhythmogenic right ventricular tachycardia; 1,037 [21%] with BrS; 28 [0.6%] with CPVT; 2,466 [50%] with hypertrophic cardiomyopathy; 162 [3.3%] with lamin A/C gene mutations; 462 [9.4%] with LQTS; and 51 [1.0%] with SQTS). Overall, inappropriate shocks occurred in 20% over a mean follow up of 51 months, corresponding to an inappropriate shock rate of 4.7% per year (95% CI 4.2 to 5.3%). Over a mean follow up of 55 months, ICD-related complications occurred in 22%, most commonly lead malfunction (10.3% of patients). The pooled rate of ICD-related complications was 4.4% per year (95% CI 3.6 to 5.2%).

SUBCUTANEOUS ICDS

Totally subcutaneous ICDs (S-ICDs) are a less invasive alternative to the conventional transvenous ICD, and are intended for patients who do have standard indications for an ICD, but who do not require pacing for bradycardia or antitachycardia overdrive pacing for VT. The S-ICD has also been proposed to be of particular benefit for patients with limited vascular access, including patients undergoing renal dialysis or children; or those who have had complications with transvenous ICDs. Evaluating the safety and efficacy of S-ICDs requires comparisons with transvenous ICDs in large, long-term, randomized, controlled trials. These comparisons are necessary to determine whether any benefits of S-ICDs outweigh risks and whether they offer advantages over transvenous ICDs with respect to the rate of adverse effects, successful termination of life-threatening arrhythmias, and unnecessary shocks.

RANDOMIZED CONTROLLED TRIALS

The Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy (PRAETORIAN) trial was a noninferiority RCT that compared S-ICD to transvenous ICD in 849 patients with an indication for ICD but no indication for pacing.[81] The trial is the only RCT on the effect of an S-ICD with health outcomes. Patients were eligible if they were 18 years and older with a class I or IIa indication for ICD therapy for primary or secondary prevention, according to professional society guidelines, and no indication for pacing. The median age of enrolled patients was 63 years (interquartile range, 55 to 70). Most enrolled patients were diagnosed with ischemic and nonischemic cardiomyopathy and 19.7% were women. The median left ventricular ejection fraction was 30%.

The primary end point in PRAETORIAN was the composite of device-related complications and inappropriate shocks. The trial was designed to test the hypothesis of noninferiority of the S-ICD as compared with the transvenous ICD with respect to the time from device implantation to the first occurrence of a primary end point event. The primary analysis was the modified intention-to-treat cohort (i.e., patients were analyzed in accordance with the treatment group to which they were originally assigned, regardless of withdrawals, losses to follow-up or crossovers). Patients who did not receive a device and patients who proved ineligible for one of the treatments due to incomplete or inadequate screening were excluded from this analysis. In the as-treated cohort, patients were analyzed in the group of the specific ICD type which

they received at initial implantation regardless of randomization result, withdrawals, losses to follow-up or crossovers. The noninferiority margin for the upper boundary of the 95% confidence interval for the HR was set at 1.45.

The trial results indicated that S-ICD was noninferior to the transvenous ICD on the composite endpoint of device-related complications and inappropriate shocks. The HR for the primary end point was 0.99 (95% CI 0.71 to 1.39, p=0.01 for noninferiority; p=0.95 for superiority). Results for the modified intention-to-treat analysis and as-treated analysis did not differ. There were more device related complications in the transvenous ICD group and more inappropriate shocks in the S-ICD group, but the trial was not powered for these endpoints. A number of secondary cardiac outcomes were also reported. There were more deaths from any cause in the S-ICD group than in the transvenous ICD group (16.4% vs. 13.1%, HR 1.23, 95% CI 0.89 to 1.70), but the number of sudden cardiac deaths did not differ between groups (18 in each group). There were more appropriate shocks in the S-ICD group (19.2% vs. 11.5%, HR 1.52, 95% CI 1.08 to 2.12). Other secondary endpoints did not differ between the groups.

While the rate of sudden cardiac death in the PRAETORIAN trial was low (18 patients in each group), the number of overall deaths was 151, and actually occurred more frequently than the composite outcome. The HR for all-cause mortality was 1.23 (95% CI 0.89 to 1.70). The PRAETORIAN trial investigators conducted competing risks analyses to account for discontinuation of follow-up before the primary end point had occurred in (1) the modified ITT population with competing risk of death, and (2) the true ITT population with competing risk of death and discontinuation of follow-up. These analyses led to consistent estimates of the HR (and 95% CI) for the primary end point. Device and lead complications occurred more frequently in the transvenous ICD group.

The choice of a composite primary endpoint poses several challenges to interpreting the results of PRAETORIAN. In this trial, the components of the composite endpoint were discordant; device-related complications were expected to favor S-ICD and inappropriate shocks were expected to favor transvenous ICD. The timing of the components of the composite outcome assessment is important in interpreting the study results and explaining expected treatment results to patients. Early benefit could favor one treatment over another, and results could change with longer follow-up. This is an important point to consider when assessing complications such as lead failure, which continue to increase over the life of the device. Additionally, because the composite was not used in earlier trials of the active comparator, there is no historical data on which to derive the expected performance of the active control. The inappropriate shock rate was based on results from the MADIT-RT trial, which compared programmed high-rate or delayed T-ICD therapy, and the expected rate of complications was based on results from MADIT-RT and the SCD-HeFT trial, which compared amiodarone to transvenous ICD. To estimate the expected event rate in PRAETORIAN, the researchers combined these two endpoints to arrive at the expected 17.2% event rate for the composite primary outcome. The study authors do not cite any previous RCTs that used the composite endpoint of complications and inappropriate shocks. All-cause mortality was a primary endpoint in several previous RCTs of transvenous ICD. However, the PRAETORIAN trial protocol (2012) noted that all-cause mortality was not chosen as the primary endpoint because "mortality event rates in both groups are presumed to be low, leading to an extremely large trial size if this would serve as a primary endpoint." The protocol also states that safety and efficacy of the S-ICD have been demonstrated in earlier trials and that the composite endpoint was "preferred above all-cause mortality, as practical, reasonably achievable, and pertinent to most cardiologists."

Another major limitation of PRAETORIAN was that the median 48-month follow-up was not long enough to determine complications over the life of the device. In fact, the PRAETORIAN study authors note in their discussion, "longer-term follow-up of this cohort will be important because the incidence of lead-related complications increases over time with the transvenous ICD and because battery longevity is a limiting factor for the subcutaneous ICD." Five-year data from the S-ICD PAS should provide more information on longer-term adverse events such as lead failure and need for device replacement.

Quality of life data from PRAETORIAN was collected but has not yet been published. This data could shed light on the relative importance to patients of adverse events such as inappropriate shocks and device replacement, especially if quality of life data were reported by subgroups of patients who experienced shocks. For example, these data might indicate that inappropriate shocks are so distressing to patients that they outweigh any potential benefits of S-ICDs.

Finally, the under-enrollment of women in the trial (19.7%) potentially limits the applicability of its results, although a subgroup analysis by sex was consistent with the primary analysis on the composite endpoint (HR in women 0.65, 95% CI 0.28 to 1.47).

NONRANDOMIZED STUDIES

Comparative Studies

Kobe (2013) published a prospective study that followed 69 patients who received S-ICD.[82] These were compared with a group of 69 sex- and age-matched patients with conventional ICD who were randomly selected from an ICD database. Fifty-four patients were followed-up over a minimum of two years. The successful conversion rate was 89.5% for S-ICD and 90.8% for transvenous ICD (p=0.81). The rate of perioperative AEs was similar for the two groups, as were the rate of inappropriate shocks (p=0.745) during short-term follow-up.

The Subcutaneous versus Transvenous Arrhythmia Recognition Testing (START) study compared the performance of a subcutaneous ICD with a transvenous ICD for detecting arrhythmias in the electrophysiology lab.[83] The patient population included 64 patients who were scheduled for ICD implantation. All patients had a transvenous ICD placed as well as subcutaneous electrodes attached to a subcutaneous ICD. Arrhythmias were induced and the sensitivity and specificity of detection by each device was compared. For ventricular arrhythmias, sensitivity of detection was 100% for the subcutaneous ICD and 99% for the transvenous ICD. Specificity was 98.0% for the subcutaneous ICD device compared to 76.7% for the transvenous device (p<0.001).

Non-comparative Studies

Gold (2021) reported 18-month data from the UNTOUCHED study, a multinational, prospective trial designed to assess the performance of the S-ICD in primary prevention patients with a low LVEF and New York Heart Association II/III heart failure or coronary artery disease.[84] At 18 months, the complication-free rate was 92.7% and the inappropriate shock-free rate was 95.9%. One-year data from the S-ICD Post Approval Study and 18-month data from the UNTOUCHED study have been published; these studies are ongoing.

The S-ICD System Post-Approval Study (PAS) is a nonrandomized, standard-of-care registry in the United States that has prospectively enrolled and followed S-ICD recipients.[85] During the first year after implantation, complications were observed in 119 patients, with a complication-free rate at one year of 92.5%. The most common complication was device

system infection in 44 of 1,637 patients. This five-year study is expected to be completed in October 2021, with a total of 1,766 participants. Five-year data from the PAS should provide more information on longer-term adverse events such as lead failure and need for device replacement.

A single-center registry study published by Mithani (2018) compared outcomes between patients implanted with S-ICD (n=91) and a matched control group implanted with a transvenous single-chamber ICD.[86] Control matching was based on gender, age, and dialysis status. The patients who received an S-ICD were more likely to be on chronic dialysis, have higher creatinine levels, and have had prior device infections compared to transvenous ICD patients. No significant difference was seen in implant complication rates or death in the six months after implantation.

Lambiase (2016) evaluated the use of the S-ICD in patients with hypertrophic cardiomyopathy in the S-ICD System Clinical Investigation (S-ICD IDE Study) and the EFFORTLESS registry (both described below), reporting on 99 patients with hypertrophic cardiomyopathy, who were compared with 773 non-hypertrophic cardiomyopathy patients.[87] At the time of reporting, three episodes of ventricular arrhythmias had been identified in the hypertrophic cardiomyopathy cohort, all of which were successfully terminated. In the hypertrophic cardiomyopathy group, 12.5% of subjects had experienced an inappropriate shock at a mean follow up of 22.0 months, which did not differ significantly from the rate in non-hypertrophic cardiomyopathy patients (10.7%, p=NS).

A follow-up publication by Boersma (2017) reported five-year outcomes for the EFFORTLESS S-ICD study. There were 82 patients that completed the five-year visit, with mean follow-up for the group of 3.1 ± 1.5 years. The rate of inappropriate shock 8.1% at one year, and 11.7% at 3.1 years, while the rate of appropriate shock was 5.8% at one year and 13.5% at five years.[88]

Boersma (2016) reported outcomes for patients in the S-ICD IDE study and the EFFORTLESS registry stratified by whether patients had been previously treated with a transvenous ICD.[89] At the time of analysis, 866 patients were available for inclusion. Of those, 75 (8.7%) were implanted with an S-ICD following transvenous ICD extraction for a system-related infection and 44 (5.1%) were implanted following transvenous ICD extraction for reasons other than a system-related infection, while the remaining 747 (86.3%) were de novo implants. Patients explanted for infection were older than patients whose transvenous ICD was explanted for non-infection related events and the de novo implant patients (55.5, 47.8, and 49.9 years, respectively, p=0.01), were more likely to have an ICD for secondary prevention (42.7%, 37.2%, and 25.6%, respectively, p<0.0001), and had a higher incidence of comorbidities. There were no significant differences in the rates of system- or procedure-related complications between patients whose transvenous ICDs were explanted for infection, those whose transvenous ICDs were explanted for non-infectious reasons, and the de novo S-ICD patients (10.7%, 6.8%, and 9.6%, respectively, p=0.078).

Another subanalysis of the pooled S-ICD IDE study and EFFORTLESS registry data, which included 882 patients at the time of analysis, evaluated the effect of learning curves on implant time, procedure complications, and inappropriate shocks.[90] Rates of complications were significantly lower in patients treated by the least experienced providers than those treated with the most experienced (9.8% vs 5.4%, p=0.02).

Theuns (2015) reported long term follow up of a cohort study.[91] Over a median follow up of 5.8 years, 26 devices (47%) were replaced and 5 (9%) were explanted. Four patients (7%)

required S-ICD explantation and replacement with a transvenous system, two due to a requirement for cardiac resynchronization therapy, one due to a requirement for bradycardia pacing, and one due to ineffective defibrillation testing. Most devices (81%) were replaced due to an elective replacement indication, at a median time to replacement of 5.0 years. Event-free rates for device replacement after 2, 4, and 6 years were 94%, 89%, and 30%, respectively. A total of 119 delivered shocks in 16 patients (29%) were recorded).

El-Chami (2015) reported on a single-center study of outcomes after S-ICD placement in patients with endstage renal disease (ESRD) undergoing chronic dialysis, which included 79 patients who underwent S-ICD placement, 27 of whom were on chronic dialysis.[92] This research was prompted by prior studies that suggested higher mortality rates for ESRD patients implanted with transvenous ICDs. The composite outcome (frequency of death, heart failure hospitalization, or appropriate S-ICD shocks) was nonsignificantly higher in the ESRD group (23.8%/year vs 10.9%/year, p=0.317), a difference that was primarily driven by a significantly higher incidence of appropriate S-ICD shocks in the ESRD group (17.9%/year vs 1.4%/year, p=0.021).

Burke (2015) published a pooled analysis of patients from the S-ICD IDE study and the EFFORTLESS registry, which included 882 patients.[93] The poolability of data across the two studies was assessed by analysis of complications, appropriate and inappropriate shocks, conversion efficacy, and mortality by study, with additional analyses for outcomes that differed by study. Patients were followed for a mean of 651 (±345) days. Most patients (63%) presented with a history of previous transvenous ICDs that required extraction due to infection. Within 30 days of the procedure, 4.5% of subjects experienced a complication, while 11.1% of subjects experienced a complication within three years of the procedure. The most common complication was infection requiring device removal/revision (17 events in 14 patients [1.7%]). Mortality was low: the annual mortality rate was 1.6% and the two-year mortality rate was 3.2%. The Kaplan-Meier incidence of time to first therapy for VT or VF was 5.3% at one year, 7.9% at two years, and 10.5% at three years. Excluding VT/VF storms, 111 discrete VT/VF events were treated, with 100 (90.1%) terminated with the first shock, and 109 (98.2%) terminated within the five shocks available. The Kaplan- Meier incidence of time to first inappropriate shock was 13.1% at three years. In patients with dual zone programming at the index procedure, the Kaplan-Meier incidence of inappropriate shock at three years was 11.7% compared with 20.5% with single-zone programming. A significant study effect was observed for inappropriate shocks (p=0.0209), with a smaller proportion of inappropriate shocks in the EFFORTLESS group, but this effect was negated after correction for initially-programmed number of zones, shock zone rate, and conditional zone rate.

Gold (2014) published a subanalysis of patients in the S-ICD IDE study to evaluate a discrimination algorithm to reduce inappropriate shocks.[94] Patients in the study could receive one of two shock detection algorithms, a single- or double-zone configuration. In the single-zone configuration, shocks are delivered for detected heart rates above the programmed rate threshold. In the dual-zone configuration, arrhythmia discrimination algorithms are active in a lower rate zone up to a shockable heart rate threshold. At hospital discharge, dual-zone programming was used in 226 subjects (72%) and single-zone programming was used in the remaining 88 subjects (28%). Inappropriate shocks occurred on 23 of 226 (10.2%) subjects with dual-zone programming and 23 of 88 (26.1%, p<0.001) subjects with single-zone programming. Freedom from appropriate shocks did not differ between groups.

Lambiase (2014) described patients in the EFFORTLESS-ICD registry, a multicenter European registry to report outcomes for patients treated with S-ICD.[95] At the time of analysis, the registry included 472 patients, 241 of whom (51%) were enrolled prospectively, at a median follow-up time of 498 days. Nine patients (2%) died during the reported period, none of the deaths, which were known to occur in the perioperative period, although the cause of death was unknown for one patient. A total of 317 spontaneous episodes in 85 patients were recorded during the follow-up, of which 169 episodes received therapy in 59 patients. Of the 145 classified untreated episodes, 93 were adjudicated as inappropriate sensing, 37 were nonsustained VT/VF, 12 were nonsustained SVT above discrimination zone, and three were unclassified. Of the VT/VF episodes, the first shock conversion efficacy was 88%, with 100% overall successful clinical conversion after a maximum of five shocks. A total of 73 inappropriate shocks were recorded in 32 patients over an average follow-up of 18 months (360-day inappropriate shock rate of 7%).

The S-ICD IDE Study was a multicenter series of 330 patients from several countries.[96] The S-ICD was successfully implanted in 314 of 330 patients (95.1%). Laboratory-induced VF was successfully terminated in more than 90% of patients, which was one of the primary outcomes of the study. The second primary outcome, greater than 99% freedom from complications at 180 days, was also met. Patients were followed for a mean duration of 11 months. There were 38 spontaneous episodes of VT in 21 patients (6.7%), and all were successfully terminated. Inappropriate shocks were received by 41 patients (13.1%).

A series of 118 patients from four centers in the Netherlands was published in 2013. Patients were followed for a mean of 18±7 months.[97] Device-related complications occurred in 14% of patients, including infection (5.9%), dislodgement of the device or leads (3.3%), skin erosion (1.7%), and battery failure (1.7%). In one patient, the S-ICD was replaced with a transvenous ICD because of the need for antitachycardia pacing. Over the entire follow-up period, eight patients experienced 45 appropriate shocks, with a first-shock conversion efficacy of 98%. Fifteen patients (13%) received a total of 33 inappropriate shocks. Two patients died, one due to cancer and one to progressive heart failure.

Aydin (2012) reported outcomes for 40 consecutive patients implanted with SICDs at three German centers.[98] Patients were considered for S-ICD if they met criteria for ICD implantation for primary or secondary prevention specified by the American College of Cardiology/American Heart Association/European Society of Cardiology, did not have symptomatic bradycardia, incessant ventricular tachycardia, or documented spontaneous, frequently-recurring ventricular tachycardia that was reliably terminated with antitachycardia pacing, and did not have pacemakers. Of the cohort, 25.0% had a prior transvenous ICD, and 57.5% received the S-ICD for secondary prevention. Over a median follow-up of 229 days, S-ICD activity was recorded in 10.0% of the patients, for whom a total of 25 episodes were retrieved. Of these, 21 shock episodes were correctly identified as ventricular tachyarrhythmia. The overall S-ICD shock efficacy was 96.4% (95% CI 12.8% to 100%).

Bardy (2010) described the development and testing of the device, including empiric evidence for the optimal placement of the subcutaneous electrode.[99] A total of 55 patients were tested in the electrophysiology lab for termination of induced arrhythmias and subsequently followed for a mean of 10.1 months for successful termination of detected arrhythmias and clinical outcomes. In the electrophysiology lab study, intraoperative VF was induced in 53 of 55. All episodes were correctly detected by the S-ICD. In 52 of 53 patients, two consecutive episodes of ventricular arrhythmia were successfully terminated. In the final patient, the arrhythmia was

terminated on one occasion but not on the other. In the cohort portion of this study, 54 of 55 patients were alive at last follow-up. The one death was due to renal failure, and this patient requested removal of the S-ICD before death. An infection at the generator site occurred in two patients, necessitating a revision procedure. Another three patients had lead dislodgement requiring repositioning. There were a total of 12 episodes of VT that were detected by the S-ICD; all 12 episodes were successfully terminated by countershock.

S-ICDS AND ADVERSE EVENTS

The systematic review and meta-analysis by Auricchio (2017), described previously, evaluated inappropriate shocks in patients with single-chamber ICDs (VR-ICDs) and S-ICDs using data from 16 articles.[79] They found an overall rate of 6.4% of patients per year received an inappropriate shock, and this risk was no significant difference associated with the use of S-ICDs or ventricular tachycardia zone programming. The authors noted that one of the included studies had an anomalously low reported rate of inappropriate shocks (1.9%), which was not explained by the study design or covariates.

Olde Nordkamp (2015) used data from the EFFORTLESS-ICD registry to evaluate rates of inappropriate shocks associated with the S-ICD.[100] The patient population at the time of publication included 581 S-ICD recipients, 48 of whom (8.3%) experienced a total of 101 inappropriate shocks over a follow up period of 21.4 months. Most inappropriate shocks (73%) were related to T-wave oversensing.

Brisben (2015) described the development of an algorithm designed to reduce T-wave oversensing by S-ICDs.[101] The algorithm was developed using 133 episodes of T-wave oversensing and 70 episodes of appropriately treated VT or VF collected from S-ICD log files and 174 VT/VF recordings from an ECG signal library. It was validated using 164 episodes of T-wave oversensing from S-ICD log files and 137 and 328 recorded episodes, respectively, of VT/VF and supraventricular tachycardia from an ECG signal library. The revised algorithm was associated with a reduction in T-wave oversensing of 39.8% (95% CI 28.4% to 51.2%, p=0.001 vs baseline.) Patient outcomes after the use of this algorithm have not been reported yet.

Groh (2014) evaluated an ECG screening test to determine patients who are potential S-ICD candidates who are at risk for T wave oversensing.[102] One hundred patients who had previously undergone transvenous ICD implantation and who were not receiving bradycardia pacing and did not have an indication for pacing were included. ECGs were obtained with lead placement to mimic the sensing vectors available on the S-ICD, and a patient was considered to qualify for S-ICD if the screening ECG template passed in any same lead supine and standing, at any gain, and without significant morphologic changes in QRS complexes. Of the included subjects who were potentially eligible for S-ICD, 8% were considered to fail based the ECG screening.

Kooiman (2014) reported inappropriate shock rates among 69 patients treated at a single center with an S-ICD between February 2009 and July 2012 who were not enrolled in one of two other concurrent trials.[103] Over a total follow-up of 1316 months (median per patient, 21 months), the annual incidence of inappropriate shocks was 10.8%. In eight patients, inappropriate shocks were related to T wave oversensing. After patients underwent adjustment of the sensing vector, no further inappropriate shocks occurred in 87.5% of patients with T wave oversensing.

ICDS WITH ST SEGMENT MONITORING

The intent of ICDs with the capability for continuous ST segment monitoring is to detect possible myocardial ischemic events. Thus, the validation of this additional feature in ICDs focuses on evidence demonstrating the following:

- Technical performance of ICD-based ischemic monitoring compared with intermittent monitoring with conventional external ECG
- Diagnostic performance (i.e., sensitivity, specificity, and positive and negative predictive value), particularly the rate of false positive detections that could lead to unnecessary testing or invasive procedures
- Clinical utility, specifically evidence that demonstrates the ability of this monitoring to improve patient health outcomes.

There are currently no randomized controlled trials for ICD-based ischemia monitoring. Two preliminary nonrandomized comparative trials have been published. Baron (2006) compared surface ECG (SECG) with intrathoracic ECG (IT-ECG) in 22 patients undergoing PTCA.[104]IT-ECG was reported to be significantly more sensitive than SECG in early and overall ischemia assessment, with highest sensitivity of 85%. However, this study did not indicate how these tests results were used in patient management to improve health outcomes. More recently, Forleo (2012) compared ICDs with (n=53) versus without (n=50) ST-segment monitoring capability.[105] After at least six months follow-up, one patient in the ST monitoring group had an ST elevation myocardial infarction three weeks after implantation, but the algorithm had not yet been activated. Seven patients in the ST monitoring group had at least one episode (range 1 to 90) of false-positive ST events; the programmable features of the device helped overcome the problem in six patients. Unscheduled outpatient visits were significantly increased in ST monitored patients with a remote monitoring system (17 vs. 4, p=0.032). The authors concluded that ICD-based ST monitoring failed to provide a benefit over ICD alone and increased unscheduled evaluations in patients with remote follow-up.

EXTRAVASCULAR (EV) ICDS

Recently, EV ICDs have been developed that rely on substernal leads for pacing. Feasibility studies have been published,[106, 107] but these devices have not been approved by the FDA and clinical trials are underway.

PRACTICE GUIDELINE SUMMARY

The following section includes the current evidence-based clinical practice guidelines for use of ICDs. Consensus statements are not included.

THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION/HEART RHYTHM SOCIETY

In 2017, the American Heart Association (AHA), American College of Cardiology (ACC), and Heart Rhythm Society (HRS) published practice guidelines on the management ventricular arrhythmia and prevention of sudden cardiac death. These guidelines made the recommendations on use of implantable cardioverter defibrillator (ICD) devices, including the the recommendations below, with a class of recommendation of I (strong recommendation) or IIa (moderate recommendation). The recommendations for use of an ICD apply only if meaningful survival is expected to be greater than one year.

Each recommendation is further classified as either A, B, or C, based on the weight of the evidence available.

- Level A is applied when data are from multiple, high-quality randomized clinical trials;
- Level B indicates data are from a moderate-quality randomized trials (B-R) or nonrandomized trials (B-NR); and
- Level C is applied when the recommendation is based lower quality evidence - either limited data (C-LD) or expert opinion (C-EO).

Transvenous ICD recommendations

For primary prevention in ischemic heart disease:

- In patients with LVEF of 35% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days postrevascularization, and with NYHA class II or III HF despite GDMT [guideline-directed medical therapy], an ICD is recommended (Class I, Level of Evidence [LOE]: A)

- In patients with LVEF of 30% or less that is due to ischemic heart disease who are at least 40 days' post-MI and at least 90 days postrevascularization, and with NYHA class I HF despite GDMT, an ICD is recommended (Class I, LOE: A)
- In patients with NSVT [nonsustained ventricular tachycardia] due to prior MI, LVEF of 40% or less and inducible sustained VT or VF at electrophysiological study, an ICD is recommended (Class I/ LOE: B-R)
- In nonhospitalized patients with NYHA class IV symptoms who are candidates for cardiac transplantation or an LVAD, an ICD is reasonable (Class IIa, LOE: B-NR)

For secondary prevention in ischemic heart disease:

- In patients with ischemic heart disease, who either survive SCA due to VT/VF or experience hemodynamically unstable VT (Class 1, LOE: B-R) or stable VT (Class I, LOE: B-NR) not due to reversible causes, an ICD is recommended
- In patients with ischemic heart disease and unexplained syncope who have inducible sustained monomorphic VT on electrophysiological study, an ICD is recommended (Class I, LOE: B-NR)
- In patients resuscitated from SCA due to coronary artery spasm in whom medical therapy is ineffective or not tolerated, an ICD is reasonable (Class IIa, LOE: B-NR)

For primary prevention in NICM:

- In patients with NICM, HF with NYHA class II–III symptoms and an LVEF of 35% or less, despite GDMT, an ICD is recommended (Class I, LOE: A)

- In patients with NICM due to a Lamin A/C mutation who have 2 or more risk factors (NSVT, LVEF <45%, nonmissense mutation, and male sex), an ICD can be beneficial (Class IIa, LOE: B-NR)

For secondary prevention in NICM:

- In patients with NICM who either survive SCA due to VT/VF or experience hemodynamically unstable VT (LOE: B-R) or stable VT (LOE: B-NR) not due to reversible causes, an ICD is recommended (Class I)

- In patients with NICM who experience syncope presumed to be due to VA and who do not meet indications for a primary prevention ICD, an ICD or an electrophysiological study for risk stratification for SCD can be beneficial (Class IIa, LOE: B-NR)

For hypertrophic cardiomyopathy:

- In patients with HCM who have survived an SCA due to VT or VF, or have spontaneous sustained VT causing syncope or hemodynamic compromise, an ICD is recommended (Class I, LOE: B-NR)
- In patients with HCM and 1 or more of the following risk factors, an ICD is reasonable: maximum LV wall thickness ≥30 mm (LOE: B-NR), SCD in 1 or more first-degree relatives presumably caused by HCM (LOE: C-LD), and 1 or more episodes of unexplained syncope within the preceding 6 months (LOE: C-LD) (Class IIa)
- In patients with HCM who have spontaneous NSVT (LOE: C-LD) or an abnormal blood pressure response with exercise (LOE: B-NR), who also have additional SCD risk modifiers or high risk features, an ICD is reasonable (Class IIa)

For cardiac sarcoidosis:

- In patients with cardiac sarcoidosis who have sustained VT or are survivors of SCA or have an LVEF of 35% or less, an ICD is recommended (Class I, LOE: B-NR)
- In patients with cardiac sarcoidosis and LVEF greater than 35% who have syncope and/or evidence of myocardial scar by cardiac MRI or positron emission tomographic (PET) scan, and/or have an indication for permanent pacing implantation of an ICD is reasonable (Class IIa, LOE: B-NR)
- In patients with cardiac sarcoidosis and LVEF greater than 35%, it is reasonable to perform an electrophysiological study and to implant an ICD, if sustained VA is inducible (Class IIa, LOE: C-LD)
- In patients with cardiac sarcoidosis who have an indication for permanent pacing, implantation of an ICD can be beneficial (Class IIa, LOE: C-LD)

For neuromuscular disorders:

- In patients with neuromuscular disorders, primary and secondary prevention ICDs are recommended for the same indications as for patients with NICM (Class I, LOE: B-NR)
- In patients with Emery-Dreifuss and limb-girdle type IB muscular dystrophies with progressive cardiac involvement, an ICD is reasonable (Class IIa, LOE: B-NR)

For cardiac channelopathies:

- In patients with a cardiac channelopathy and SCA, an ICD is recommended (Class I, LOE: B-NR)
- In high-risk patients with symptomatic long QT syndrome in whom a beta blocker is ineffective or not tolerated, intensification of therapy with additional medications (guided by consideration of the particular long QT syndrome type), left cardiac sympathetic denervation, and/or an ICD is recommended (Class I, LOE: B-NR)
- In patients with catecholaminergic polymorphic ventricular tachycardia and recurrent sustained VT or syncope, while receiving adequate or maximally tolerated beta blocker, treatment intensification with either combination medication therapy (e.g., beta blocker, flecainide), left cardiac sympathetic denervation, and/or an ICD is recommended (Class I, LOE: B-NR)

- In patients with Brugada syndrome with spontaneous type 1 Brugada electrocardiographic pattern and cardiac arrest, sustained VA or a recent history of syncope presumed due to VA, an ICD is recommended (Class I, LOE: B-NR)
- In patients with early repolarization pattern on ECG and cardiac arrest or sustained VA, an ICD is recommended (Class I, LOE: B-NR)
- In patients with short QT syndrome who have a cardiac arrest or sustained VA, an ICD is recommended (Class I, LOE: B-NR)

For adult congenital heart disease:

- In patients with adult congenital heart disease and hemodynamically unstable VT, an ICD is recommended after evaluation and appropriate treatment for residual lesions/ventricular dysfunction (Class I, LOE: B-NR)
- In patients with adult congenital heart disease with SCA due to VT or VF in the absence of reversible causes, an ICD is recommended (Class I, LOE: B-NR)
- In adults with repaired tetralogy of Fallot physiology and inducible VT/VF or spontaneous sustained VT, implantation of an ICD is reasonable (Class IIa, LOE: B-NR)
- In patients with repaired moderate or severe complexity adult congenital heart disease with unexplained syncope and at least moderate ventricular dysfunction or marked hypertrophy, either ICD implantation or an electrophysiological study with ICD implantation for inducible sustained VA is reasonable (Class IIa, LOE: B-NR)

For other indications:

- In patients resuscitated from SCA due to coronary artery spasm in whome medical therapy is ineffective or not tolerated, an ICD is reasonable (Class IIa, LOE: B-NR)
- In patients with arrhythmogenic right ventricular cardiomyopathy and an additional marker of increased risk of SCD (resuscitated SCA, sustained VT, significant ventricular dysfunction with RVEF or LVEF ≤35%), an ICD is recommended (Class I, LOE: B-NR)
- In patients with arrhythmogenic right ventricular cardiomyopathy and syncope presumed due to VA, an ICD can be useful (Class IIa, LOE: B-NR)
- In patients with HFrEF who are awaiting heart transplant and who otherwise would not qualify for an ICD (e.g., NYHA class IV and/or use of inotropes) with a plan to discharge home, an ICD is reasonable (Class IIa, LOE: B-NR)
- In patients with an LVAD and sustained VA, an ICD can be beneficial (Class IIa, LOE: C-LD)
- In patients resuscitated from SCA due to idiopathic polymorphic VT or VF, an ICD is recommended (Class I, LOE: B-NR)

Subcutaneous ICD recommendations:

- In patients who meet criteria for an ICD who have inadequate vascular access or are at high risk for infection, and in whom pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated, a subcutaneous implantable cardioverter-defibrillator is recommended (Class I, LOE: B-NR)
- In patients who meet indication for an ICD, implantation of a subcutaneous implantable cardioverter-defibrillator is reasonable if pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated (Class IIa, LOE: B-NR)

AMERICAN HEART ASSOCIATION/AMERICAN COLLEGE OF CARDIOLOGY

In 2020, the American Heart Association and American College of Cardiology published a joint Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy, which included the following recommendations:[108]

- For patients with HCM, and previous documented cardiac arrest or sustained ventricular tachycardia, ICD placement is recommended. (Class I, LOE: B-NR)
- For adult patients with HCM with 1 or more major risk factors for SCD, it is reasonable to offer an ICD. (Class IIa, LOE: B-NR)
- For children with HCM who have 1 or more conventional risk factors, ICD placement is reasonable after considering the relatively high complication rates of long-term ICD placement in younger patients. (Class IIa, LOE: B-NR)
- For patients 16 years and older with HCM and 1 or more major SCD risk factors, discussion of the estimated 5-year sudden death risk and mortality rates can be useful during the shared decision-making process for ICD placement. (Class IIa, LOE: B-NR)
- In patients with HCM without risk factors, ICD placement should not be performed. (Class III: Harm, LOE: B-NR)
- In patients with HCM, ICD placement for the sole purpose of participation in competitive athletics should not be performed. (Class III: Harm, LOE: B-NR)
- In patients with hypertrophic cardiomyopathy who are receiving an ICD, either a single chamber transvenous ICD or a subcutaneous ICD is recommended after a shared decision-making discussion that takes into consideration patient preferences, lifestyle, and expected potential need for pacing for bradycardia or ventricular tachycardia termination. (Class I, LOE: B-NR)

HEART RHYTHM SOCIETY (HRS)

Arrhythmogenic Cardiomyopathy

In 2019, the HRS published a consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy (ACM).[109] Recommendations related to ICD risk stratification and placement decisions include the following:

- Class I (strong) recommendations:
  - In individuals with ACM with LVEF 35% or lower and NYHA class II-III symptoms and an expected meaningful survival of greater than 1 year, an ICD is recommended. (LOE: B-R)
  - In individuals with ACM (other than ARVC) and hemodynamically tolerated VT, an ICD is recommended. (LOE: B-NR)
- Class IIa (moderate) recommendations:
  - In individuals with ARVC with hemodynamically tolerated sustained VT, an ICD is reasonable. (LOE: B-NR)
  - ICD implantation is reasonable for individuals with ARVC and three major, two major and two minor, or one major and four minor risk factors for ventricular arrhythmia. (LOE: B-NR)
  - In individuals with ACM with LVEF 35% or lower and NYHA class I symptoms and an expected meaningful survival of greater than 1 year, an ICD is reasonable. (LOE: B-R)
  - In individuals with phospholamban cardiomyopathy and LVEF <45% or NSVT, an ICD is reasonable. (LOE: B-R)

- o In individuals with lamin A/C ACM and two or more of the following: LVEF <45%, NSVT, male sex, an ICD is reasonable. (LOE: B-R)
- o In individuals with FLNC ACM and an LVEF <45%, an ICD is reasonable. (LOE: C-LD)
- o In individuals with lamin A/C ACM and an indication for pacing, an ICD with pacing capabilities is reasonable. (LOE: C-LD)
- Class IIb (weak) recommendations:
  - o ICD implantation may be reasonable for individuals with ARVC and two major, one major and two minor, or four minor risk factors for ventricular arrhythmia. (B-NR)

Cardiac Sarcoid

In 2014, the HRS published a consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis, including recommendations for ICD implantation in patients with cardiac sarcoid.[110] The writing group concluded that although there are few data specific to ICD use in patients with cardiac sarcoid, data from the major primary and secondary prevention ICD trials were relevant to this population and recommendations from the general device guideline documents apply to this population.

PEDIATRIC AND CONGENITAL ELECTROPHYSIOLOGY SOCIETY (PACES)/HRS

In 2014, PACES and HRS issued an expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease (CHD) which made the following recommendations on the use of ICD therapy in adults with CHD:[111]

- Class I recommendations:

  - o ICD therapy is indicated in adults with CHD who are survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable ventricular tachycardia after evaluation to define the cause of the event and exclude any completely reversible etiology (LOE: B).
  - o ICD therapy is indicated in adults with CHD and spontaneous sustained ventricular tachycardia who have undergone hemodynamic and electrophysiologic evaluation (LOE: B).
  - o ICD therapy is indicated in adults with CHD and a systemic left ventricular ejection fraction <35%, biventricular physiology, and New York Heart Association (NYHA) class II or III symptoms (LOE: B).

- Class IIa recommendations:

  - o ICD therapy is reasonable in selected adults with tetralogy of Fallot and multiple risk factors for sudden cardiac death, such as left ventricular systolic or diastolic dysfunction, nonsustained ventricular tachycardia, QRS duration>180 ms, extensive right ventricular scarring, or inducible sustained ventricular tachycardia at electrophysiologic study (LOE: B).

- Class IIb recommendations:

  - o ICD therapy may be reasonable in adults with a single or systemic right ventricular ejection fraction <35%, particularly in the presence of additional risk factors such as

complex ventricular arrhythmias, unexplained syncope, NYHA functional class II or III symptoms, QRS duration >140 ms, or severe systemic AV valve regurgitation (LOE: C)

- o ICD therapy may be considered in adults with CHD and a systemic ventricular ejection fraction <35% in the absence of overt symptoms (NYHA class I) or other known risk factors (LOE of: C).
- o ICD therapy may be considered in adults with CHD and syncope of unknown origin with hemodynamically significant sustained ventricular tachycardia or fibrillation inducible at electrophysiologic study (LOE: B).
- o ICD therapy may be considered for nonhospitalized adults with CHD awaiting heart transplantation (LOE: C).
- o ICD therapy may be considered for adults with syncope and moderate or complex CHD in whom there is a high clinical suspicion of ventricular arrhythmia and in whom thorough invasive and noninvasive investigations have failed to define a cause (LOE: C).

- Class III recommendations:

  - o All Class III recommendations listed in current ACC/AHA/HRS guidelines apply to adults with CHD (LOE: C).
  - o Adults with CHD and advanced pulmonary vascular disease (Eisenmenger syndrome) are generally not considered candidates for ICD therapy (LOE: B).
  - o Endocardial leads are generally avoided in adults with CHD and intracardiac shunts. Risk assessment regarding hemodynamic circumstances, concomitant anticoagulation, shunt closure prior to endocardial lead placement, or alternative approaches for lead access should be individualized (LOE: B).

SUMMARY

TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDS)

Pediatric Patients

There is enough research to show that implantable cardioverter defibrillators (ICDs) can improve survival for pediatric patients that are at increased risk of cardiac events. Therefore, the use of ICDs may be considered medically necessary for pediatric patients.

Patients with Prior Arrhythmogenic Events and Ischemic Cardiomyopathy

There is enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for certain patients that have had arrhythmogenic events and ischemic cardiomyopathy. A number of clinical guidelines based on research recommend these ICDs for patients meeting specific criteria. Therefore, the use of ICDs may considered medically necessary for patients that meet the policy criteria.

There is not enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve health outcomes for patients with ischemic cardiomyopathy that do not meet the policy criteria. This includes people who have had a myocardial infarction (heart attack) in the past 40 days, people with a relatively high level of heart function. Therefore, the use of ICDs in ischemic cardiomyopathy patients that do not meet the policy criteria is considered investigational.

Heart Failure

There is enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for certain heart failure patients, including patients with a reduced ejection fraction who will be discharged home to await heart transplantation, and patients with NYHA *Class IV* symptoms that are candidates for a left ventricular assist device or heart transplantation. Clinical guidelines based on research recommend ICDs for patients meeting these criteria. Therefore, the use of ICDs may be considered medically necessary for heart failure patients that meet the policy criteria.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes for patients with heart failure patients that do not meet the policy criteria. This includes people who have had a myocardial infarction (heart attack) in the past 40 days, people with a relatively high level of heart function, and people with NYHA *Class IV* symptoms that are not eligible to receive a combination cardiac resynchronization therapy ICD device, left ventricular assist device, or cardiac transplantation. Therefore, the use of ICDs in patients that do not meet the policy criteria is considered investigational.

Nonischemic Cardiomyopathy (NICM)

There is enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for certain patients with nonischemic cardiomyopathy (NICM) and certain neuromuscular disorders that affect heart function. Also, clinical guidelines based on research recommend ICD use for these patients. Therefore, ICD implantation among patients with NICM or neuromuscular disorders that meet the policy criteria may be considered medically necessary.

There is not enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for patients with nonischemic cardiomyopathy (NICM) or neuromuscular disorders that do not meet policy criteria, including patients that have a treatable cause for their NICM. Therefore, ICD use in these patients is considered investigational.

Hypertrophic Cardiomyopathy

There is enough research to show that implantable cardioverter defibrillators (ICDs) can improve survival in some patients with hypertrophic cardiomyopathy (HCM). There are also clinical guidelines based on research that recommend ICDs for certain patients with HCM. Therefore, ICD implantation among patients with HCM that meet policy criteria may be considered medically necessary.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes for people with hypertrophic cardiomyopathy (HCM) that do not have major risk factors for sudden cardiac death. Therefore, ICD use is considered investigational for patients with HCM that do not meet the policy criteria.

LMNA-related Cardiac Arrhythmia or Cardiomyopathy

There is enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes compared with pacemakers or medical treatment in patients with *LMNA*-related cardiac arrhythmias or cardiomyopathy. Because of the high risk for sudden

cardiac death, ICDs may be considered medically necessary in patients with *LMNA* gene mutations that have cardiomyopathy or symptomatic arrhythmias, or have certain risk factors.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients with *LMNA* gene mutations that do not have cardiomyopathy, symptomatic arrhythmias, or specific risk factors, and therefore, the use of ICDs among these patients is considered investigational.

Cardiac Ion Channelopathies

There is enough research to show that implantable cardioverter defibrillators (ICDs) can reduce sudden cardiac death in certain patients with long QT syndrome, short QT syndrome, Brugada syndrome, or catecholaminergic polymorphic ventricular tachycardia. Clinical guidelines based on research also recommend ICD therapy in patients with these conditions that have other cardiac risk factors. Therefore, ICDs may be considered medically necessary in select patients with cardiac ion channelopathies.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients with cardiac ion channelopathies that do not have certain cardiac risk factors, and therefore, the use of ICDs among these patients is considered investigational.

Cardiac Sarcoidosis

There is enough research to show that implantable cardioverter defibrillators (ICDs) can reduce sudden cardiac death in certain patients with cardiac sarcoidosis. Clinical guidelines based on research also recommend ICD therapy in patients with this condition that have other cardiac risk factors. Therefore, ICDs may be considered medically necessary in select patients with cardiac sarcoidosis.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients with cardiac sarcoidosis that do not have certain cardiac risk factors, and therefore, the use of ICDs among these patients is considered investigational.

ICDs for Secondary Prevention

There is enough research to show that implantable cardioverter defibrillators (ICDs) can be effective for *secondary* prevention in certain patients, including those that have had life-threatening ventricular arrhythmia not caused by a reversible condition. Therefore, ICD use may be considered medically necessary for secondary prevention in these patients.

There is not enough research to show that implantable cardioverter defibrillators (ICDs) can improve health outcomes in patients that have had arrhythmia events caused by reversible conditions, and ICD use is therefore considered investigational for these patients.

SUBCUTANEOUS ICDS

There is enough research to show that subcutaneous implantable cardioverter defibrillators (S-ICDs) can improve health outcomes in patients that may benefit from ICD use, and have

no indications for antibradycardia or antitachycardia pacing. Therefore, the use of S-ICDs may be considered medically necessary for the same indications as transvenous ICDs.

There is not enough research to show that subcutaneous implantable cardioverter defibrillators (S-ICDs) use can improve health outcomes in people who do not meet policy criteria for transvenous ICD placement, and people with indications for antibradycardia or antitachycardia pacing. Therefore, S-ICD placement is considered investigational for patients that do not meet policy criteria for transvenous ICD placement and patients that may require antibradycardia or antitachycardia pacing.

ICDS WITH ST SEGMENT MONITORING CAPABILITY

There is not enough research to show that implantable cardioverter defibrillators (ICDs) with ST segment monitoring capability can improve health outcomes compared to traditional transvenous ICDs. Also, there are no ICDS with segment monitoring capabilities that have received U.S. Food and Drug Administration (FDA) approval for marketing in the U.S. Therefore, the use of implantable cardioverter defibrillators with ST segment monitoring capability is considered investigational for all indications.

EXTRAVASCULAR (EV) ICDS

There is not enough research to show that extravascular implantable cardioverter defibrillators (EV ICDs), also known as substernal ICDs, improve health outcomes compared to traditional transvenous or subcutaneous ICDs. Also, there are no EV ICDs that have received U.S. Food and Drug Administration (FDA) approval for marketing in the U.S. Therefore, the use of EV ICDs is considered investigational for all indications

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112. BlueCross BlueShield Association Medical Policy Reference Manual "Implantable Cardioverter Defibrillator (ICD)." Policy No. 7.01.44

CODES

Codes	Number	Description
CPT	0571T	Insertion or replacement of permanent implantable cardioverter defibrillator system, with substernal electrode(s), including all imaging guidance defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters, when performed
	0572T	Insertion of substernal implantable defibrillator electrode
	0573T	Removal of substernal implantable defibrillator electrode
	0574T	Repositioning of previously implanted extravascular substernal implantable defibrillator-pacing electrode
	0575T	Programming device evaluation (in person) of implantable cardioverter defibrillator system with substernal electrode, with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional
	0576T	Interrogation device evaluation (in person) of implantable cardioverter defibrillator system with substernal electrode, with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter
	0577T	Electrophysiologic evaluation of implantable cardioverter defibrillator system with substernal electrode (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)
	0578T	Interrogation device evaluation(s) (remote), up to 90 days, substernal lead implantable cardioverter defibrillator system w/interim analysis, review(s) and report(s) by a physician or other qualified health care professional
	0579T	Interrogation device evaluation(s) (remote), up to 90 days, substernal lead implantable cardioverter defibrillator system, remote data acquisition(s), receipt of transmissions and technician review, technical support and distribution of results
	0580T	Removal of substernal implantable defibrillator pulse generator only
	0614T	Removal and replacement of substernal implantable defibrillator pulse generator

Codes	Number	Description
	33216	Insertion of a single transvenous electrode, permanent pacemaker or cardioverter-defibrillator
	33217	Insertion of 2 transvenous electrodes, permanent pacemaker or cardioverter-defibrillator
	33218	Repair of single transvenous electrode for a single chamber, permanent pacemaker or single chamber pacing cardioverter-defibrillator
	33220	Repair of 2 transvenous electrodes for a dual chamber permanent pacemaker or dual chamber pacing cardioverter-defibrillator
	33223	Relocation of skin pocket for cardioverter-defibrillator
	33230	Insertion of pacing cardioverter-defibrillator pulse generator only; with existing dual leads
	33231	Insertion of pacing cardioverter-defibrillator pulse generator only; with existing multiple leads
	33240	Insertion of single or dual chamber pacing cardioverter-defibrillator pulse generator
	33241	Removal of implantable defibrillator pulse generator only
	33243	Removal of single or dual chamber implantable defibrillator electrode(s); by thoracotomy
	33244	;by transvenous extraction
	33249	Insertion or replacement of permanent implantable defibrillator system, with transvenous lead(s), single or dual chamber
	33262	Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; single lead system
	33263	;dual lead system
	33264	;multiple lead system
	33270	Insertion or replacement of permanent subcutaneous implantable defibrillator system, with subcutaneous electrode, including defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters, when performed
	33271	Insertion of subcutaneous implantable defibrillator electrode
	33272	Removal of subcutaneous implantable defibrillator electrode
	33273	Repositioning of previously implanted subcutaneous implantable defibrillator electrode
HCPCS	C1721	Cardioverter-defibrillator, dual chamber (implantable)
	C1722	Cardioverter-defibrillator, single chamber (implantable)
	C1882	Cardioverter-defibrillator, other than single or dual chamber (implantable)

Date of Origin: *April 2012*