Implantable Cardioverter Defibrillator

Effective: August 1, 2017

Next Review: April 2018
Last Review: April 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

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

Note:

- This policy addresses only initial ICD implantation; it does not address ICD removal or replacement.
- This policy does not address ICD implantation in pediatric patients less than 18 years of age, which may be considered medically necessary.

Transvenous Implantable Cardioverter Defibrillator (ICD)
A The use of the *transvenous* automatic implantable cardioverter defibrillator (ICD) may be considered **medically necessary** in patients 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 (1 or 2):

1. For primary prevention when at least one of the following criteria (a.-i.) are met:
   a. Ischemic cardiomyopathy with New York Heart Association (NYHA) functional *Class I* symptoms when both of the following criteria (i and ii) are met:
      i. History of myocardial infarction at least 40 days before ICD treatment; and
      ii. Left ventricular ejection fraction of 30% or less

   *NYHA Class I = No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).

   b. Ischemic cardiomyopathy with NYHA functional *Class II* symptoms when both of the following criteria (i and ii) are met:
      i. History of myocardial infarction at least 40 days before ICD treatment; and
      ii. Left ventricular ejection fraction of 35% or less

   **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

   c. Nonischemic dilated cardiomyopathy when all of the following criteria (i - iii) 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

   d. Hypertrophic cardiomyopathy (HCM) at high risk for sudden cardiac death with at least one of the following major risk factors:
      i. History of premature HCM-related sudden death in one or more first-degree relatives younger than 50 years; or
      ii. Left ventricular hypertrophy greater than 30 mm; or
      iii. One or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour holter monitoring; or
iv. Prior unexplained syncope inconsistent with neurocardiogenic origin

e. Documented *LMNA* gene mutations (lamin A/C deficiency) in patients with at least one of the following conditions:
   i. Cardiomyopathy; or
   ii. Symptomatic cardiac arrhythmias

f. Diagnosis of long QT syndrome (LQTS) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Recurrent syncopal events while on beta blocker therapy

g. Diagnosis of Brugada syndrome (BrS) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Spontaneous sustained ventricular tachycardia (VT) with or without syncope; or
   iii. Spontaneous diagnostic type 1 ECG with a history of syncope, seizure, or nocturnal agonal respiration after noncardiac causes have been excluded; or
   iv. Development of ventricular fibrillation (VF) during programmed electrical stimulation

h. Diagnosis of catecholaminergic polymorphic ventricular tachycardia (CPVT) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Recurrent syncope; or
   iii. Polymorphic/bidirectional VT that is nonresponsive to medical management, or left cardiac sympathetic denervation

i. Diagnosis of short QT syndrome (SQTS) with at least one of the following:
   i. Prior cardiac arrest; or
   ii. Symptomatic and have documented spontaneous VT with or without syncope; or
   iii. Family history of sudden cardiac death

2. For *secondary* prevention in patients with a 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.

B. The use of the *transvenous* ICD is considered *investigational* when Criteria I.A. are not met and including, but not limited to, patients with any of the following:
1. Have had an acute myocardial infarction (i.e., less than 40 days before ICD treatment); or
2. Have New York Heart Association (NYHA) Class IV**** congestive heart failure (unless patient is eligible to receive a combination cardiac resynchronization therapy ICD device); or
   ****NYHA Class IV = inability to carry on any activity without symptoms; symptoms may be present at rest
3. 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
4. Have noncardiac disease that would be associated with life expectancy less than 1 year

II Subcutaneous Implantable Cardioverter Defibrillator (ICD)
   A The use of the subcutaneous ICD may be considered medically necessary in patients who meet all of the following criteria (1-4):
      1. Applicable medical necessity criteria for transvenous ICD is met (Criteria I.); and
      2. Have a contraindication to a transvenous ICD due to at least one of the following (a-c):
         a. Lack of adequate vascular access; or
         b. The need to preserve existing vascular access due to chronic dialysis; or
         c. Repeat transvenous ICD placement not indicated due to complications with previous transvenous ICD placement;
      3. Have no indication for antibradycardia pacing; and
      4. Do not have ventricular arrhythmias that are known or anticipated to respond to antitachycardia pacing
   B The use of the subcutaneous ICD is considered investigational when the above criteria (II. A.) are not met.

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

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

CROSS REFERENCES
1. Wearable Cardioverter-Defibrillators as a Bridge to Implantable Cardioverter-Defibrillator Placement, Durable Medical Equipment, Policy No 61.
2. Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy, Genetic Testing, Policy No. 72

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 sternal. 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.

**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 Fortify™ ST ICD (St. Jude Medical, Inc.) has received investigational device exemption (IDE) clearance from the FDA for use only in the clinical trial setting.
• 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.

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.

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 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. Wolff et al. meta-analyzed five RCTs with a total of 2992 dilated cardiomyopathy patients that compared ICD therapy with medical therapy for primary prevention.[2] They found a significant reduction in mortality and sudden cardiac death with ICD therapy (odds ratio [OR], 0.77; 95% CI, 0.64-0.93; p = 0.006 and OR, 0.43; 95% CI, 0.27-0.69; p = 0.0004, respectively). Similarly, Luni et al. performed a meta-analysis of six RCTs evaluating ICD use for primary prevention in patients with nonischemic cardiomyopathy.[3] 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 et al. included only four RCTs, as they included only trials that compared ICD to medical therapy that included at least 100 nonischemic cardiomyopathy patients and had follow-up periods of at least 12 months.[4] This analysis also reported a significant mortality reduction with ICD therapy (hazard ratio [HR], 0.75; 95% CI, 0.61-0.93; P = .008).

In 2014 Gracieux et al. 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.[5] 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.[6] 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 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\[7-23\]) and four cohort studies\[24-27\] 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 sudden cardiac death (SCD) was rated as high. These studies found reduced risk of all-cause mortality 3-7 years after ICD implantation and SCD 2-6 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\[28-31\] 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) ≤35%. Most of the studies excluded adults over 70-80 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 NICM.

Chen et al. (2013) analyzed eight RCTs\[28,32-50\] that compared the safety and effectiveness of ICD alone with cardiac resynchronization therapy and ICD (CRT-D) in patients with heart failure.\[51\] 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 6 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 3-6 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.

In a 2012 Shinkel et al. reported the results of a systematic review and meta-analysis of 16 studies of patients with ICDs for hypertrophic cardiomyopathy (HCM).[55] 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 >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 was 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 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)**

Kober et al. 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 cardiac resynchronization therapy (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, 0.29-0.92). The risk for cardiovascular death was also not significantly different between groups (hazard ratio [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, 0.31-0.82). 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**
Nonischemic Dilated Cardiomyopathy

Amara et al. (2017) compared ICD therapy for the prevention of sudden cardiac death in patients with nonischemic (NICM) and ischemic (ICM) cardiomyopathy enrolled in the multicenter Défibrillateur Automatique Implantable-Prévention Primaire (DAI-PP) study. A total of 5485 patients participated in the study, 2181 (39.8%) with NICM and 3304 (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.

A meta-analysis of five trials including nonischemic subjects reported a statistically significant reduction in mortality associated with ICD therapy. Furthermore, when the body of evidence for ICD therapy in both ischemic and nonischemic populations is considered together, the preponderance of evidence suggests that ICD therapy improves health outcomes compared with medical management alone with a relative risk reduction in all-cause mortality between 21% and 35%. While the risk of adverse events (AEs) is not well-reported in studies of patients without prior MI, it seems reasonable to expect similar low rates of device-related AEs as seen in studies of patients with prior MI.

Hypertrophic Cardiomyopathy

In 2015, Magnusson et al. reported outcomes for 321 patients with HCM treated with an ICD enrolled in a Swedish registry. 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 1 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.

Adverse Effects

Ezzat et al. (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. The review included 18 RCTs with a total of 6796 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% (91% 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 et al., in a population-based cohort study including all Danish patients who underwent a cardiac implantable electronic device procedure from 2010-2011 (562/5918 patients [9.5%] with at least 1 complication).[59]

Persson et al. (2014) published a systematic review and meta-analysis of AEs following ICD implantation.[60] 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.[6] The rate of early adverse events was 2.8-3.6% during hospitalization, of which 1.2-1.35% 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 <0.1-6.4% 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 1-5 years follow-up occurred in 3-21% 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 et al. (2017) focused on inappropriate shocks from both single chamber ICDs (VR-ICDs) and subcutaneous ICDs (S-ICDs).[61] The review included 16 articles, which showed that an average of 6.4% (95% CI, 5.1-7.9%) 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.

ICDS IN PATIENTS WITH LMNA GENE MUTATION

In a systematic review for GeneReviews®, Hershberger et al. 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.”[62]

Pasotti et al. conducted a retrospective longitudinal study with 94 individuals with mutations in the LMNA gene.[63] 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 ventricular tachycardia). 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

In 2010, Horner et al. 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. 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

Conte et al. 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. Before ICD implantation, 14.2% of subjects had a history of aborted sudden cardiac death (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 et al. reported results of a Portuguese registry that included 55 patients with Brugada syndrome, 36 of whom were treated with ICDs for either primary or secondary prevention. 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, 7 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 Brugada syndrome treated with ICDs, Steven et al. reported that 2/3 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. In a smaller registry that included 25 patients with Brugada syndrome treated with ICDs, over an average follow up of 41.2 months, appropriate shocks were delivered in 3 patients, all of whom had prior cardiac arrest.

### Catecholaminergic Polymorphic Ventricular Tachycardia

Roston et al. reported results of a multicenter retrospective cohort study that included 226 patients with catecholaminergic polymorphic ventricular tachycardia. 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 9 (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 3 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 et al. reported results of a small retrospective study of 13 patients with CPVT who received an ICD.[70] The indication for ICD therapy was syncope despite maximal beta-blocker therapy in 6 patients (46%) and aborted SCD in 7 patients (54%). Over a median follow-up of 4.0 years, 10 patients (77%) received a median 4 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.

Adverse Effects

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.

In 2016, Olde Nordkamp et al. reported on a systematic review and meta-analysis of studies reporting on ICD complications in individuals with inherited arrhythmia syndromes.[71] The review included 63 cohort studies with a total of 4916 patients (710 [10%] with arrhythmogenic right ventricular tachycardia; 1037 [21%] with BrS; 28 [0.6%] with CPVT; 2466 [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

No randomized controlled trials of S-ICDs have been published.
Nonrandomized Studies

Comparative Studies

In 2013, Kobe et al. prospectively followed 69 patients who received S-ICD.[72] 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 adverse events were similar between 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.[73] 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

In 2016, Lambiase et al. evaluated the use of the S-ICD in patients with hypertrophic cardiomyopathy in the S-ICD IDE study and the EFFORTLESS registry, reporting on 99 patients with hypertrophic cardiomyopathy, who were compared with 773 non-hypertrophic cardiomyopathy patients.[74] 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).

In 2015, Boersma et al. 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.[75] 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.[76] 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).

In 2015, Theuns et al. reported long term follow up of the Bardy cohort.[77] 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, 2 due to a requirement for cardiac resynchronization therapy, 1 due to a requirement for bradycardia pacing, and 1 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 et al. 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 SICD placement, 27 of whom were on chronic dialysis.[78] 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).

In 2015 Burke et al. published a pooled analysis of patients from the S-ICD IDE study and the EFFORTLESS registry, which included 882 patients.[79] 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 3 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 2-year mortality rate was 3.2%. The Kaplan-Meier incidence of time to first therapy for VT or VF was 5.3% at 1 year, 7.9% at 2 years, and 10.5% at 3 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 5 shocks available. The Kaplan-Meier incidence of time to first inappropriate shock was 13.1% at 3 years. In patients with dual zone programming at the index procedure, the Kaplan-Meier incidence of inappropriate shock at 3 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 et al. published a subanalysis of patients in the S-ICD IDE study to evaluate a discrimination algorithm to reduce inappropriate shocks.[80] Patients in the study could receive 1 of 2 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.

A large study was reported by Lambiase et al. who described patients in the EFFORTLESS-ICD registry, a multicenter European registry to report outcomes for patients treated with S-ICD.[81] 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 1 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 3 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%).

A large series was a multicenter study 330 patients from several countries, the S-ICD System Clinical Investigation (S-ICD IDE Study).[82] 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 4 centers in the Netherlands was published in 2013. Patients were followed for a mean of 18±7 months.[83] 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 1 patient, the S-ICD was replaced with a transvenous ICD because of the need for antitachycardia pacing. Over the entire follow-up period, 8 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, 1 due to cancer and 1 to progressive heart failure.

Aydin et al. reported outcomes for 40 consecutive patients implanted with SICDs at 3 German centers.[84] 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 et al. described the development and testing of the device, including empiric evidence for the optimal placement of the subcutaneous electrode, in 2010.[85] 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, 2 consecutive episodes of ventricular arrhythmia were successfully terminated. In the final patient, the arrhythmia was terminated on 1 occasion but not on the other. In the cohort portion of this study, 54 of 55 patients were alive at last follow-up. The 1 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 2 patients, necessitating a revision procedure. Another 3 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.

Adverse Effects

The systematic review and meta-analysis by Auricchio et al. evaluated inappropriate shocks in patients with single-chamber ICDs (VR-ICDs) and S-ICDs using data from 16 articles.[61] 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 et al. used data from the EFFORTLESS-ICD registry to evaluate rates of inappropriate shocks associated with the S-ICD.[86] 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 et al. described the development of an algorithm designed to reduce T-wave oversensing by S-ICDs.[87] 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 et al. evaluated an ECG screening test to determine patients who are potential S-ICD candidates who are at risk for T wave oversensing.[88] 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 et al. 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 1 of 2 other concurrent trials.[89] Over a total follow-up of 1316 months (median per patient, 21 months), the
annual incidence of inappropriate shocks was 10.8%. In 8 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. In 2006, Baron et al. compared surface ECG (SECG) with intrathoracic ECG (IT-ECG) in 22 patient undergoing PTCA.[90]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 et al. compared ICDs with (n=53) versus without (n=50) ST-segment monitoring capability.[91] After at least 6 months follow-up, one patient in the ST monitoring group had an ST elevation myocardial infarction 3 weeks after implantation, but the algorithm had not yet been activated. Seven patients in the ST monitoring group had at least one episode (range 1-90) 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.

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 (ACC/AHA/HRS) GUIDELINES

The 2012[92] ACC/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities updates the 2008[93] Guideline for Implantation of Cardiac Pacemakers and Antiarrhythmic Devices. Guideline recommendations are classified into three levels: Classes I, II, and III. Class I is defined as “conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.” Only Class I recommendations are listed here. 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, randomized clinical trials; level B is when data are from a limited number of
The 2008 guidelines of the ACC/AHA/HRS for implantation of cardiac pacemakers and antiarrhythmia devices include the following Class I indications for ICDs:

1. ICD therapy is indicated in patients who are survivors of cardiac arrest due to ventricular fibrillation (VF) or hemodynamically unstable sustained ventricular tachycardia (VT) after evaluation to define the cause of the event and to exclude any completely reversible causes. (Level of Evidence: A)
2. ICD therapy is indicated in patients with structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable. (Level of Evidence: B)
3. ICD therapy is indicated in patients with syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study. (Level of Evidence: B)
4. ICD therapy is indicated in patients with LVEF less than 35% due to prior MI who are at least 40 days post-MI and are in NYHA functional Class II or III. (Level of Evidence: A)
5. ICD therapy is indicated in patients with NIDCM who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III. (Level of Evidence: B)
6. ICD therapy is indicated in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF less than 30%, and are in NYHA functional Class I. (Level of Evidence: A)
7. ICD therapy is indicated in patients with nonsustained VT due to prior MI, LVEF less than 40%, and inducible VF or sustained VT at electrophysiological study. (Level of Evidence: B)

ACC/AHA GUIDELINES ON THE DIAGNOSIS AND MANAGEMENT OF HEART FAILURE

In 2013 the ACC/AHA issued practice guidelines on the management of heart failure which made the recommendations below about the use of ICDs as primary prevention[94]. The following guideline recommendations are classified into three levels: Classes I, IIa, IIb, and III.

- Class I: Procedure/treatment is considered useful/effective and is recommended.
- Class IIa: Procedure is reasonable to perform but additional studies are needed
- Class IIb: Procedure may be considered; usefulness is unknown or not well established
- Class III No Benefit: Procedure is not recommended/indicated.
- Class III Harm: Procedure should not be performed; potentially harmful or associated with excess morbidity/mortality.

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, randomized clinical trials;
- Level B indicates data are from a limited number of randomized trials; and
- Level C is applied when the recommendation is primarily based on expert consensus.

For patients with stage B heart failure, an ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 days post-MI, have an LVEF ≤30%, are on appropriate medical therapy, and have reasonable expectation of survival with a good functional status for > 1 year. (Class of recommendation: IIa; Level of Evidence: B)

For patients with stage C heart failure, ICD therapy is recommended for:
• Primary prevention of SCD in select patients with NIDCM or ischemic heart disease at least 40 days post-MI with LVEF ≤ 35%, and NYHA Class II or III symptoms for > 1 year. (Class of recommendation: I; Level of Evidence: A)

• Primary prevention of SCD to reduce total mortality in selected patients at least 40 days post-MI with LVEF < 30%, and NYHA class I symptoms while receiving guideline-directed medical therapy (GDMT), who have reasonable expectation of (Class of recommendation: I; Level of Evidence: B)

• An ICD is of uncertain benefit to prolong meaningful survival in patients with a high risk of non-sudden death such as frequent hospitalizations, advanced frailty, or comorbidities such as systemic malignancy or severe renal dysfunction. (Class of recommendation: IIb; Level of Evidence: B)

AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION/AMERICAN HEART ASSOCIATION

In 2011, ACCF/AHA guidelines were published on the management of patients with hypertrophic cardiomyopathy.[95] These guidelines contained the following statements about the use of ICDs in patients with HCM:

• Class I Recommendations
  o The decision to place an ICD in patients with HCM should include application of individual clinical judgment, as well as a thorough discussion of the strength of evidence, benefits, and risks to allow the informed patient’s active participation in decision making. (Level of Evidence: C)
  o ICD placement is recommended for patients with HCM with prior documented cardiac arrest, ventricular fibrillation, or hemodynamically significant VT. (Level of Evidence: B)

• Class IIa Recommendations
  o It is reasonable to recommend an ICD for patients with HCM with:
    ▪ Sudden death presumably caused by HCM in 1 or more first-degree relatives.155 (Level of Evidence: C)
    ▪ A maximum LV wall thickness greater than or equal to 30 mm. (Level of Evidence: C)
    ▪ One or more recent, unexplained syncopal episodes. (Level of Evidence: C)
  o An ICD can be useful in select patients with NSVT [non-sustained VT] (particularly those <30 years of age) in the presence of other SCD risk factors or modifiers. (Level of Evidence: C)
  o An ICD can be useful in select patients with HCM with an abnormal blood pressure response with exercise in the presence of other SCD risk factors or modifiers. (Level of Evidence: C)

• Class IIb Recommendations
  o The usefulness of an ICD is uncertain in patients with HCM with isolated bursts of NSVT when in the absence of any other SCD risk factors or modifiers. (Level of Evidence: C)
  o The usefulness of an ICD is uncertain in patients with HCM with an abnormal blood pressure response with exercise when in the absence of any other SCD risk factors or
modifiers, particularly in the presence of significant outflow obstruction. (Level of Evidence: C)

- **Class III Recommendations: Harm**
  - ICD placement as a routine strategy in patients with HCM without an indication of increased risk is potentially harmful. (Level of Evidence: C)
  - ICD placement as a strategy to permit patients with HCM to participate in competitive athletics is potentially harmful. (Level of Evidence: C)
  - ICD placement in patients who have an identified HCM genotype in the absence of clinical manifestations of HCM is potentially harmful. (Level of Evidence: C)

**THE HEART FAILURE SOCIETY OF AMERICA/HEART RHYTHM SOCIETY/EUROPEAN HEART RHYTHM ASSOCIATION**

In 2009 the HFSA, HRS and EHRA published a guideline for the management of genetic cardiomyopathies that included specific mention of LMNA-related DCM:[96]

- In patients with cardiomyopathy and significant arrhythmia or known risk of arrhythmia an ICD may be considered before the left ventricular ejection fraction falls below 35%. (Level of evidence = C)

The guideline states: “In this setting of lamin A/C cardiomyopathy requiring pacemaker placement, the use of an ICD rather than a pacemaker has been recommended. Patients with a dilated cardiomyopathy but with ejection fraction >30% to 35% may be considered for an ICD if the family history is positive for SCD or for patients with LMNA mutations.”

**PEDIATRIC AND CONGENITAL ELECTROPHYSIOLOGY SOCIETY (PACES)/HEART RHYTHM SOCIETY (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:[97]

- **Class I Recommendations:**
  - 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 (Level of evidence: B).
  - ICD therapy is indicated in adults with CHD and spontaneous sustained ventricular tachycardia who have undergone hemodynamic and electrophysiologic evaluation (Level of evidence: B).
  - 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 (Level of evidence: B).

- **Class IIa Recommendations:**
  - 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 (Level of evidence: B).

- **Class IIb Recommendations:**
  - 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 (Level of evidence: C).
  - 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 (Level of evidence: C).
  - 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 (Level of evidence: B).
  - ICD therapy may be considered for nonhospitalized adults with CHD awaiting heart transplantation (Level of evidence: C).
  - 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 (Level of evidence: C).

- **Class III Recommendations:**
  - All Class III recommendations listed in current ACC/AHA/HRS guidelines apply to adults with CHD (Level of evidence: C).
  - Adults with CHD and advanced pulmonary vascular disease (Eisenmenger syndrome) are generally not considered candidates for ICD therapy (Level of evidence: B).
  - 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 (Level of Evidence: B).

HEART RHYTHM SOCIETY/EUROPEAN HEART RHYTHM ASSOCIATION/ASIA-PACIFIC HEART RHYTHM SOCIETY

In 2013, the Heart Rhythm Society (HRS), European Heart Rhythm Association (EHRA), and the Asia-Pacific Heart Rhythm Society (APHRS) issued a consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes, which included a number of recommendations related to ICD use in patients with long QT syndrome (LQTS), Brugada syndrome (BrS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and short QT syndrome (SQTS).

**Long QT Syndrome**

- **Class I Recommendations**
  - ICD implantation is recommended for patients with a diagnosis of LQTS who are survivors of a cardiac arrest.

- **Class IIa Recommendations**
ICD implantation can be useful in patients with a diagnosis of LQTS who experience recurrent syncopal events while on beta-blocker therapy.

- **Class III Recommendations: Harm**
  - Except under special circumstances, ICD implantation is not indicated in asymptomatic LQTS patients who have not been tried on beta-blocker therapy.

**Brugada Syndrome**

- **Class I Recommendations:**
  - ICD implantation is recommended in patients with a diagnosis of BrS who:
    - Are survivors of a cardiac arrest and/or
    - Have documented spontaneous sustained VT with or without syncope.

- **Class IIa Recommendations:**
  - ICD implantation can be useful in patients with a spontaneous diagnostic type I ECG who have a history of syncope judged to be likely caused by ventricular arrhythmias.

- **Class IIb Recommendations:**
  - ICD implantation may be considered in patients with a diagnosis of BrS who develop VF during programmed electrical stimulation (inducible patients).

- **Class III Recommendations: Harm**
  - ICD implantation is not indicated in asymptomatic BrS patients with a drug-induced type I ECG and on the basis of a family history of SCD alone.

**Catecholaminergic Polymorphic Ventricular Tachycardia**

- **Class I Recommendations:**
  - ICD implantation is recommended for patients with a diagnosis of CPVT who experience cardiac arrest, recurrent syncope or polymorphic/bidirectional VT despite optimal medical management, and/or left cardiac sympathetic denervation.

- **Class III Recommendations: Harm**
  - ICD as a standalone therapy is not indicated in an asymptomatic patient with a diagnosis of CPVT.

**Short QT Syndrome**

- **Class I Recommendations:**
  - ICD implantation is recommended in symptomatic patients with a diagnosis of SQTS who:
    - Are survivors of cardiac arrest and/or
    - Have documented spontaneous VT with or without syncope.
Class IIb Recommendations:

- ICD implantation may be considered in asymptomatic patients with a diagnosis of SQTS and a family history of sudden cardiac death.

HEART RHYTHM SOCIETY/EUROPEAN HEART RHYTHM ASSOCIATION

In a consensus report from the second consensus conference on Brugada syndrome, held in September 2003, HRS/EHRA addressed diagnostic criteria, risk stratification schemes, and device- and pharmacologic-based therapy for Brugada syndrome. This report was published in 2005 and makes the following recommendations for ICD implantation in Brugada syndrome:

- Symptomatic patients displaying the type 1 Brugada ECG (either spontaneously or after sodium channel blockade) who present with aborted sudden death should receive an ICD without additional need for electrophysiologic studies.
- Symptomatic patients displaying the type 1 Brugada ECG (either spontaneously or after sodium channel blockade) who present with syncope, seizure, or nocturnal agonal respiration should undergo ICD implantation after noncardiac causes of these symptoms have been ruled out.
- Asymptomatic patients displaying a type 1 Brugada ECG (either spontaneously or after sodium channel blockade) should undergo EPS if a family history of sudden cardiac death is suspected to be the result of Brugada syndrome. EPS is justified when the family history is negative for sudden cardiac death if the type 1 ECG occurs spontaneously. If inducible for ventricular arrhythmia, then the patient should receive an ICD.
- Asymptomatic patients who have no family history and who develop a type 1 ECG only after sodium channel blockade should be closely followed up.

SUMMARY

TRANSVENOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDS)

ICDs in 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 is 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.

ICDs for Nonischemic Dilated Cardiomyopathy (NIDCM)

There is enough research to show that transvenous implantable cardioverter defibrillators (ICDs) can improve survival for certain patients with nonischemic dilated cardiomyopathy (NIDCM). Also, clinical guidelines based on research recommend ICD use for some
patients with NIDCM. Therefore, ICD implantation among patients with NIDCM 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 dilated cardiomyopathy (NIDCM) that do not meet policy criteria, including patients that have a treatable cause for their NIDCM. 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 is 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.

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 or symptomatic arrhythmias, and therefore, the use of ICDs among these patients is considered investigational.

**ICDs for Patients with 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 are 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.

**ICDs for Secondary Prevention**
There is enough research to show that implantable cardioverter defibrillators (ICDs) can be effective for secondary prevention in patients 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, but for whom transvenous ICD placement is not recommended for medical reasons. Therefore, the use of S-ICDs is 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 compared with transvenous ICD use. Therefore, S-ICD placement is considered investigational for patients that do not meet policy criteria for ICD placement and patients that are candidates for transvenous ICD placement.

**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.

**REFERENCES**

5. Gracieux, J, Sanders, GD, Pokorney, SD, Lopes, RD, Thomas, K, Al-Khatib, SM. Incidence and predictors of appropriate therapies delivered by the implantable


37. Administration, USFaD. Summary of Safety and Effectiveness Data. [cited 05/19/2016]; Available from: http://www.accessdata.fda.gov/cdrh_docs/pdf3/P030054b.pdf


51. Chen, S, Ling, Z, Kiuchi, MG, Yin, Y, Krucoff, MW. The efficacy and safety of cardiac resynchronization therapy combined with implantable cardioverter defibrillator for heart


97. Khairy, P, Van Hare, GF, Balaji, S, et al. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology (ACC), the American Heart Association (AHA), the European Heart Rhythm Association (EHRA), the Canadian Heart Rhythm Society (CHR), and the International Society for Adult Congenital Heart Disease (ISACHD). The Canadian journal of cardiology. 2014 Oct;30(10):e1-e63. PMID: 25262867


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

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>33216</td>
<td>Insertion of a single transvenous electrode, permanent pacemaker or cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33217</td>
<td>Insertion of 2 transvenous electrodes, permanent pacemaker or cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33218</td>
<td>Repair of single transvenous electrode for a single chamber, permanent pacemaker or single chamber pacing cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33220</td>
<td>Repair of 2 transvenous electrodes for a dual chamber permanent pacemaker or dual chamber pacing cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33223</td>
<td>Relocation of skin pocket for cardioverter-defibrillator</td>
</tr>
<tr>
<td></td>
<td>33230</td>
<td>Insertion of pacing cardioverter-defibrillator pulse generator only; with existing dual leads</td>
</tr>
<tr>
<td>Codes</td>
<td>Number</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>33231</td>
<td>Insertion of pacing cardioverter-defibrillator pulse generator only; with existing multiple leads</td>
<td></td>
</tr>
<tr>
<td>33240</td>
<td>Insertion of single or dual chamber pacing cardioverter-defibrillator pulse generator</td>
<td></td>
</tr>
<tr>
<td>33241</td>
<td>Removal of implantable defibrillator pulse generator only</td>
<td></td>
</tr>
<tr>
<td>33243</td>
<td>Removal of single or dual chamber implantable defibrillator electrode(s); by thoracotomy</td>
<td></td>
</tr>
<tr>
<td>33244</td>
<td>;by transvenous extraction</td>
<td></td>
</tr>
<tr>
<td>33249</td>
<td>Insertion or repositioning of electrode lead(s) for single or dual chamber pacing cardioverter-defibrillator and insertion of pulse generator</td>
<td></td>
</tr>
<tr>
<td>33262</td>
<td>Removal of implantable defibrillator pulse generator with replacement of implantable defibrillator pulse generator; single lead system</td>
<td></td>
</tr>
<tr>
<td>33263</td>
<td>;dual lead system</td>
<td></td>
</tr>
<tr>
<td>33264</td>
<td>;multiple lead system</td>
<td></td>
</tr>
<tr>
<td>33270</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>33271</td>
<td>Insertion of subcutaneous implantable defibrillator electrode</td>
<td></td>
</tr>
<tr>
<td>33272</td>
<td>Removal of subcutaneous implantable defibrillator electrode</td>
<td></td>
</tr>
<tr>
<td>33273</td>
<td>Repositioning of previously implanted subcutaneous implantable defibrillator electrode</td>
<td></td>
</tr>
<tr>
<td>93260</td>
<td>Programming device evaluation (in person) 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; implantable subcutaneous lead defibrillator system</td>
<td></td>
</tr>
<tr>
<td>93261</td>
<td>Interrogation device evaluation (in person) with analysis, review and report by a physician or other qualified health care professional, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system</td>
<td></td>
</tr>
<tr>
<td>93644</td>
<td>Electrophysiologic evaluation of subcutaneous implantable defibrillator (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)</td>
<td></td>
</tr>
</tbody>
</table>

**HCPCS**

<table>
<thead>
<tr>
<th>Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1721</td>
<td>Cardioverter-defibrillator, dual chamber (implantable)</td>
</tr>
<tr>
<td>C1722</td>
<td>Cardioverter-defibrillator, single chamber (implantable)</td>
</tr>
<tr>
<td>C1882</td>
<td>Cardioverter-defibrillator, other than single or dual chamber (implantable)</td>
</tr>
</tbody>
</table>

**Date of Origin:** April 2012