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Medical Policy Manual

Topic: Implantable Cardioverter Defibrillator

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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).

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.

Regulatory Status

Several automatic ICDs are approved by the U.S. Food and Drug Administration (FDA) through the premarket application (PMA) approval 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 Guidant are approved by the FDA for use "in patients at high risk of sudden cardiac death due to ventricular arrhythmias and who have experienced at least 1 of the following: an episode of cardiac arrest (manifested by the loss of consciousness) due to a ventricular tachyarrhythmia; recurrent, poorly tolerated sustained ventricular tachycardia (VT); or a prior myocardial infarction (MI), left ventricular ejection fraction of less than or equal to 35%, and a documented episode of nonsustained VT, with an inducible ventricular tachyarrhythmia." These indications were expanded by the FDA on July 18, 2002 to include prophylactic use for cardiac patients who have had a previous heart attack and have an ejection fraction that is less than or equal to 30%. This expanded indication is based on the results of the second Multicenter Automatic Defibrillator Implantation Trial (MADIT II trial), which is discussed below.
- Medtronic devices are approved "to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias."
- Other devices with similar approval language include devices from Biotronik, Boston Scientific, St. Jude Medical, and Sorin Crm USA.

The following are examples of FDA-approved subcutaneous ICDs:

- The Subcutaneous Implantable Defibrillator (S-ICD®) System (Cameron Health, 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*.

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

MEDICAL POLICY CRITERIA

I. *Transvenous* Implantable Cardioverter Defibrillator (ICD) in Adults

A. The use of the *transvenous* automatic implantable cardioverter defibrillator (ICD) may be considered **medically necessary** in adults 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-d) 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

      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 or Class III*** symptoms when both of the following criteria (i and ii) are met:

      i. History of myocardial infarction at least 40 days before ICD treatment

      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

      ii. Reversible causes have been excluded

      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

      ii. Left ventricular hypertrophy greater than 30 mm

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

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

ii. Symptomatic cardiac arrhythmias

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** in primary prevention in patients who have one or more of the following risk factors:

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

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);

***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 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. *Transvenous* Implantable Cardioverter Defibrillator (ICD) Pediatrics

A. The use of the *transvenous* ICD may be considered **medically necessary** in children who meet at least one of the following criteria:

1. Survivor of cardiac arrest, after reversible causes have been excluded;

2. Symptomatic, sustained ventricular tachycardia in association with congenital heart disease in patients who have undergone hemodynamic and electrophysiologic evaluation; or

3. Congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias.

B. The use of the ICD is considered **investigational** for all other indications in pediatric patients.

III. The use of the following ICDs in adults or children is considered **investigational** for all indications:

A. Subcutaneous ICDs (e.g., S-ICD®)

B. ICDs with an ST-segment monitoring feature

SCIENTIFIC EVIDENCE

Implantable Cardiac Defibrillator (ICD) Use in the Adult Population

The scientific evidence evaluating the use of automatic ICDs on health outcomes in adults consists of several technology assessments and clinical trials. Evidence from well-conducted randomized controlled trials 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.

Technology Assessments

- A 2002 BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC) Assessment focused on the Multicenter Automatic Defibrillator Implantation Trials (known as MADIT I and MADIT II), which compared the use of an ICD with conventional therapy among patients with coronary artery disease with a prior history of myocardial infarction (MI) and a current history of a reduced ejection fraction.[1] The key difference in the 2 trials was the patient selection criteria. In the MADIT I trial, patients were required to have a left-ventricular ejection fraction (LVEF) of less than 35% but also ventricular tachyarrhythmia, as evidenced on an electrophysiologic study. In the subsequent, MADIT II, trial, patients were required to have a lower ejection fraction, less than 30%, but no electrophysiologic study was required. Therefore, the patient selection criteria of the MADIT II trial potentially identify a much larger number of candidates for ICD implantation.

  The TEC Assessment concluded that for patients who have coronary artery disease with prior MI and reduced LVEF and who are similar to those selected in MADIT I and MADIT II, the available evidence demonstrates an improvement in overall mortality associated with ICD treatment compared with conventional therapy.

- A 2004 BCBSA TEC Assessment focused on the results of the 5 randomized clinical trials (RCTs) included in the 2002 Assessment (including the Multicenter Unsustained Tachycardia Trial [MUSTT], MADIT I, MADIT II, Coronary Artery Bypass Graft [CABG] Patch Trial, and the Cardiomyopathy Trial [CAT]) and 5 additional RCTs:[2]

  1. Defibrillator in Acute Myocardial Infarction Trial (DINAMIT);
  2. Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)
  3. Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION);
  4. Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE); and
  5. Amiodarone versus Implantable Defibrillator Randomized Trial (AMIOVIRT).

The 2004 TEC Assessment made the following observations:

Patients Who Have Prior MI and Reduced LVEF

The previous 2002 TEC Assessment concluded that the evidence was sufficient to demonstrate that ICD therapy improves net health outcome in patients with prior MI and reduced LVEF. Both new studies (SCD-HeFT and COMPANION) and the re-analysis of MUSTT findings provide additional supportive evidence of improved outcomes in patients with prior MI. The hazard ratio (HR) for all-cause mortality in the ischemic subgroup of SCD-HeFT was 0.79 (95% confidence interval [CI] 0.60 to 1.04), which is close to that observed in MADIT II (HR: 0.69, 95% CI: 0.51 to 0.93). These findings provide additional supportive evidence that ICD therapy reduces mortality. There may be slight but not statistically significantly increased rates of adverse effects associated with ICD therapy; however, serious device-related events are not common. On balance, the significant reductions in mortality associated with ICD therapy outweigh the harms associated with ICD therapy in comparison to conventional treatment. Thus, the available evidence again demonstrates that ICD therapy improves health outcomes in patients with coronary artery disease, prior MI, and reduced LVEF.

Patients Who Have Acute MI and Reduced LVEF

The available evidence was insufficient to permit conclusions regarding the effect of ICD therapy on net health outcome for this indication.

Patients Who Have No Prior MI and Reduced LVEF (e.g., Nonischemic Dilated Cardiomyopathy, NIDCM)

Results from subjects with NIDCM included in SCD-HeFT and DEFINITE suggest a mortality benefit from ICD therapy, although statistical significance that was not achieved in these studies was likely related to insufficient power. 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 is not well-reported in studies of patients without prior MI, it seems reasonable to expect similar low rates of device-related adverse events as seen in studies of patients with prior MI.

Device-Related Adverse Effects

Device-related adverse effects were inconsistently reported in the available trials, although serious adverse events appear to be uncommon. What is known about device-related adverse effects does not outweigh the significant mortality benefits demonstrated in various studies.

Therefore, the 2004 TEC Assessment made the following conclusions:

ICD placement has been performed and investigated in multiple centers throughout the United States, and when performed by similarly experienced personnel, it is reasonable to expect that the improvements observed in the investigational setting will be attainable outside the investigational settings.

Therefore, the use of ICD devices meets the TEC criteria in the prevention of sudden death from ventricular tachyarrhythmia in patients who have:

- Symptomatic* ischemic dilated cardiomyopathy with a history of MI at least 40 days before ICD treatment and LVEF of 35% or less; or
- Symptomatic* nonischemic dilated cardiomyopathy for more than 9 months' duration and LVEF of 35% or less.

The use of ICD devices does not meet the TEC criteria in the prevention of sudden death from ventricular tachyarrhythmia in patients who:

- have had an acute MI (i.e., less than 40 days before ICD treatment);
- have New York Heart Association (NYHA) Class IV congestive heart failure (unless patient is eligible to receive a combination cardiac resynchronization therapy ICD device);
- have had cardiac revascularization procedure in past 3 months (coronary artery bypass graft [CABG] or percutaneous transluminal coronary angioplasty [PTCA]) or are candidates for a cardiac revascularization procedure; or
- have noncardiac disease that would be associated with life expectancy less than 1 year.

* Symptomatic heart failure is defined as the presence of dyspnea on exertion, angina, palpitations, or fatigue.

Further analysis of existing trial data using patient-level meta-analysis may further delineate which subgroups of patients are likely to benefit from ICD placement and those unlikely to benefit who can be spared the morbidity of ICD placement.

Randomized Controlled Trials (RCTs)

Two studies have been published since the release of the 2004 TEC assessment and are detailed below.

- The BEST-ICD (Beta-blocker Strategy + ICD) trial randomized 143 patients 5–30 days after acute MI to evaluate whether electrophysiology studies were useful to guide ICD placement and improve outcomes in patients at high risk of sudden death.[3] Entry criteria included an LVEF less than or equal to 35% along with 1 or more non-invasive risk factors (e.g., premature ventricular contractions, heart rate variability, signal-averaged electrocardiography [SAECG]-positive) and be given maximal tolerated beta-blocker (metoprolol) therapy. The authors concluded that using electrophysiology studies to guide ICD placement within 5–30 days after MI did not significantly improve outcomes and survival. This is consistent with the conclusions that ICD placement after early MI does not improve outcomes. The authors also noted that the study screened more than 15,000 patients but ended after randomizing only 12% of the targeted study population, largely because there were far fewer patients with LVEF less than 35% than expected based on experience reported in the literature.

- The Immediate Risk Stratification Improves Survival (IRIS) trial evaluated ICD implantation early after MI.[4] Eligible patients were required to have an LVEF 40% or less and either: 1) a heart rate 90 or more beats per minute on initial electrocardiogram (ECG), or 2) nonsustained ventricular tachycardia during Holter monitoring, or both. From 92 centers and 62,944 patients post-MI, 898 were randomized 5 to 31 days following the MI to ICD implantation or medical therapy. Seventy-seven percent had experienced ST elevation MI, of whom 72% underwent PTCA. During a mean

37-month follow-up, overall mortality was similar in the two arms (ICD vs. medical therapy, HR 1.04; 95% CI: 0.81 to 1.35). However, the risk of sudden cardiac death was lower following ICD (HR 0.52; 95% CI: 0.35 to 0.78), but non-sudden cardiac death risk was greater (HR 1.8; 95% CI: 1.0 to 3.2). These results are consistent with guidelines and previous trials.

Non-randomized Studies

Nonischemic Dilated Cardiomyopathy
For patients with NIDCM, the optimal timing of ICD implantation remains uncertain. Some experts consider patients with recently diagnosed NIDCM and either sustained VT or unexplained syncope to be candidates for earlier ICD implantation due to their higher risk of lethal arrhythmias. However, evidence on this specific population is lacking, and the natural history of patients in this category is not well-characterized. A substantial percent of patients diagnosed with NIDCM improve following initial diagnosis, even when a reversible cause of NIDCM cannot be identified.

- Kadish et al.[5] performed a post-hoc analysis of the DEFINITE trial data to examine whether the time from diagnosis of nonischemic dilated cardiomyopathy (NIDCM) was associated with the magnitude of benefit from ICD implantation. Survival benefit was found only for those diagnosed less than 9 months prior to implantation (n=216); no benefit was apparent when NIDCM was diagnosed greater than 9 months prior (n=242). However, there was a significant discrepancy between arms in the time from diagnosis to randomization—standard therapy patients were randomized a median of 20 months after diagnosis, while those in the ICD arm had a median of 8 months. The trial was neither designed nor powered to examine a time effect, and the analyses conflict with findings of the smaller (n=104) Cardiomyopathy (CAT) trial[6] reviewed in the 2002 TEC Assessment. Further evidence is necessary to define when in the natural history of the disease ICD implantation is appropriate.

  The Definite trial enrolled NIDCM patients without regard to time since onset, and a post-hoc analysis revealed that the benefit was found mainly in patients with onset of NIDCM for less than 9 months. Neither of these pieces of evidence represents strong data to support a specific time interval prior to implanting an ICD in patients with NIDCM.

- Zecchin et al. performed a cohort study on 503 consecutive patients diagnosed with idiopathic NIDCM to determine the extent to which indications for an ICD evolved over the several months following an initial NIDCM diagnosis.[7] At initial diagnosis, 245 met Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) criteria for an ICD, based on an ejection fraction less than 35% and Class II-III heart failure, and 258 did not meet criteria for an ICD. At a mean follow-up of 5.4 months during which patients were treated with angiotensin-converting enzyme inhibitors and beta blockers, there were consistent improvements in ejection fraction and symptoms, such that less than one-third of evaluable patients (31%) still had indications for ICD. Of patients who initially did not have an indication for an ICD, a total of 10% developed indications for an ICD at follow-up. This study highlights the fact that a decision for ICD implantation should not be made prior to optimal treatment and stabilization of patients with newly diagnosed NIDCM, since the indications for ICD are not stable over time and will change in a substantial numbers of patients following treatment.

- Ellenbogen et al. performed a sub-group analysis of NIDCM patients included in the DEFINITE trial and concluded that approximately one half of arrhythmias terminated by appropriate ICD discharges are not life-threatening.[8] The NNTBs calculated, therefore, represent lower bounds or greatest potential benefit, and the true benefit is likely less (only 6.3% of primary prevention patients had

more than one appropriate discharge).[8] Adverse events rates included one or more inappropriate discharges (27%); infections (3.8%); hemorrhage or thrombosis (1.6%); lead fractures, dislodgement, and oversensing (6.7%). While the number of risk factors present was not associated with cumulative probability to first appropriate discharge for primary prevention, patient selection for ICD implantation was performed by experienced clinicians. These results, obtained outside the setting of a clinical trial, apply under such conditions.

- Sheppard et al reported registry data on 373 subjects with recent onset NIDCM, six months or less of symptoms, and LVEF of 40% or less. Survival was comparable for patients who received ICD within one month, for those who did not receive an ICD at one month, and those who did not receive an ICD within six months. There was no significant difference in sudden cardiac deaths for patients with (0.9%) or without (1.9%) an ICD (p=0.50). The authors concluded that early ICD placement did not impact survival.

Given the current available evidence, it is not possible to predict which patients with idiopathic NIDCM will improve, nor is it possible to accurately estimate the time course for improvement. The specification of a 9-month waiting period prior to ICD implantation arises from the selection criteria of the CAT trial[6] which restricted enrollment to patients with onset of NIDCM within 9 months. While the results of this trial did not show a benefit for patients with recent onset of NIDCM, the trial was stopped early due to an unexpectedly low rate of events and was thus underpowered to detect a difference in mortality between groups. Additional RCTs, of sufficient size and duration, are needed to establish the time interval before ICD implantation.

High-Risk Hypertrophic Cardiomyopathy

- Maron and colleagues reported appropriate ICD discharge rates (terminating either ventricular tachycardia or fibrillation) from an international registry of high-risk hypertrophic cardiomyopathy (HCM) patients enrolled at 42 referral and nonreferral institutions.[9] Between 1986 and 2003, ICDs were implanted in 506 patients with HCM—383 for primary prevention and 123 for secondary prevention. The mean age of patients was 42 years (SD: 17), and 28% were 30 years of age or younger; 36% were female; mean follow-up was 3.7 years (SD: 2.8). Criteria considered in the study placing patients at high risk and, therefore, candidates for primary prevention included: 1) history of premature HCM-related sudden death in 1 or more first-degree relatives younger than 50 years of age; 2) left-ventricular hypertrophy greater than 30 mm; 3) one or more runs of nonsustained ventricular tachycardia at heart rates of 120 beats per minute or greater on 24-hour Holter monitoring; and 4) prior unexplained syncope inconsistent with neurocardiogenic origin. Abnormal exercise blood pressure was not reported. In the primary prevention group, appropriate discharges occurred at an annual rate of 3.6% (95% CI: 2.7% to 4.8%), in the secondary prevention group 10.6% (95% CI: 7.9% to 13.9%); respective 5-year cumulative probabilities of first appropriate discharge were 17% and 39%. If each appropriate discharge was life-saving, 5-year numbers needed to benefit (NNTBs) could be as low as 5.9 and 2.6 for primary and secondary prevention, respectively, when considering only the first appropriate discharge.

- Al-Khatib and Curtis published an analysis of whether ICD implantations in the U.S. followed evidence-based guidelines using a Medicare ICD registry.[10] There were a total of 111,707 patients who received an ICD between January 2006 and June 2009. Of these, 25,145 (22.5%) did not meet the evidence-based criteria according to ACC/AHA/HRS guidelines[11]. Patients who did not meet evidence-based ICD criteria had a higher mortality than patients who did meet criteria (0.57% vs. 0.18%, respectively; p<0.001) and also had a higher rate of procedural complications (3.2 vs. 2.4%,

respectively; p<0.001). Electrophysiologists had a lower rate of non-evidence-based ICD use compared to non-electrophysiologists (20.8% vs. 24.8%, respectively; p<0.001).

Adverse Effects

Several publications offered evidence on complications from ICD implantation.

- Ricci et al evaluated the incidence of lead failure in a cohort study of 414 patients implanted with an ICD with Sprint-Fidelis leads.[12] Patients were followed for a median of 35 months. Lead failures occurred in 9.7% (40/414) of patients, for an annual rate of 3.2% per patient-year. Most of the lead failures (87.5%) were due to lead fracture. The median time until recognition of lead failure, or until an adverse event, was 2.2 days. A total of 22 patients (5.3%) received an inappropriate shock due to lead failure.

- Cheng et al. examined the rate of lead dislodgements in patients enrolled in a national cardiovascular registry.[13] Of 226,764 patients treated with an ICD between April 2006 and September 2008, lead dislodgement occurred in 2,628 (1.2%). Factors associated with lead dislodgement were NYHA Class IV heart failure, atrial fibrillation/flutter, a combined ICD-CRT device, and having the procedure performed by a non-electrophysiologist. Lead dislodgement was associated with an increased risk for other cardiac adverse events and death.

- Lee et al. evaluated the rate of early complications among patients enrolled in a prospective, multi-center population-based registry of all newly implanted ICDs in Ontario, Canada from February 2007 through May 2009.[14] Of 3,340 patients receiving an ICD, major complications (lead dislodgement requiring intervention, myocardial perforation, tamponade, pneumothorax, infection, skin erosion, hematoma requiring intervention) within 45 days of implantation occurred in 4.1% of new implants. Major complications were more common in women, in patients who received a combined ICD-CRT device, and in patients with a left ventricular end-systolic size of larger than 45 mm. Direct implant-related complications were associated with a major increase in early death (HR 24.9, p<0.01).

- Two publications reported on infection rates in patients receiving an ICD. Smit et al. published a retrospective, descriptive analysis of the types and distribution of infections associated with ICDs over a 10-year period in Denmark.[15] Of 91 total infections identified, 39 (42.8%) were localized pocket infections, 26 (28.6%) were endocarditis, 17 (18.7%) were ICD-associated bacteremic infections, and 9 (9.9%) were acute post-surgical infections.

- Nery et al. reported the rate of ICD-associated infections among consecutive patients treated with an ICD at a tertiary referral center.[16] There were a total of 24 infections among 2,417 patients for a rate of 1.0%. Twenty-two of 24 patients with infections (91.7%) required device replacement. Factors associated with infection were device replacement (versus de novo implantation) and use of a complex device (e.g., combined ICD-CRT or dual/triple chamber devices).

- Sohail et al performed a case-control study evaluating the risk factors for infection in 68 patients with an ICD infection and 136 matched controls.[17] On multivariate analysis, the presence of epicardial leads (odds ratio [OR]: 9.7, p=0.03) and postoperative complications at the insertion site (OR: 27.2, p<0.001) were significant risk factors for early infection. For late-onset infections, prolonged hospitalization for >3 days (OR: 33.1 p<0.001 for 2 days vs. 1 day) and chronic obstructive pulmonary disease (OR: 9.8, p=0.02) were significant risk factors.

ICD Use in the Pediatric Population

There is limited direct scientific evidence on the efficacy of ICDs in the pediatric population. The majority of published studies in this area are retrospective analyses of small case series. A review of some of the representative publications of this type is summarized below.

- The largest published series was a combined series of pediatric patients and patients with congenital heart disease from 4 clinical centers.[18] The median age of this population was 16 years, although some adults were included up to the age of 54 years. A total of 443 patients were included. The most common diagnoses were tetralogy of Fallot and hypertrophic cardiomyopathy. ICD implantation was performed for primary prevention in 52% of patients and for secondary prevention in 48%. Over a 2-year period of follow-up, appropriate shocks occurred in 26% of patients and inappropriate shocks occurred in 21%.

- Silka et al. compiled a database of 125 pediatric patients treated with an ICD, through query of the manufacturers of commercially available devices.[19] Indications for ICD placement were survivors of cardiac arrest in 95 patients (76%), drug-refractory ventricular tachycardia in 13 patients (10%), and syncope with heart disease plus inducible ventricular tachycardia in 13 patients (10%). During a mean follow-up of 31 +/- 23 months, 73 patients (59%) received at least one appropriate shock and 25 patients (20%) received at least one inappropriate shock. The actuarial rates of sudden-death-free survival were 97% at one year, 95% at 2 years, and 90% at 5 years.

- Alexander et al. reported on 90 ICD procedures in 76 young patients with a mean age of 16 years (range: 1–30).[20] Indications for placement were 27 patients (36%) with cardiac arrest or sustained ventricular tachycardia, 40 patients (53%) with syncope, 17 patients (22%) with palpitations, 40 patients (53%) with spontaneous ventricular arrhythmias, and 36 patients (47%) with inducible ventricular tachycardia. Numerous patients had more than one indication for ICD in this study. Over a median of 2 years' follow-up, 28% of patients received an appropriate shock, and 25% of patients received an inappropriate shock.

- Lewandowski et al. reported on long-term follow-up of 63 patients between the ages of 6-21 years who were treated with an ICD device.[21] After a 10-year follow-up, there were 13 (21%) patients with surgical infections. Fourteen patients (22%) experienced at least one appropriate shock and 17 patients (27%) had at least one inappropriate shock. Serious psychological sequelae developed in 27 patients (43%).

Results from studies of ICDs among pediatric populations should be interpreted with caution as the lack of an adequate comparison group does not allow for the isolation of treatment effect from the many types of bias that can affect study outcomes. Comparative clinical trials are needed to ensure the treatment effect demonstrated among some adult populations can be safely generalized to pediatric patients.

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."[22]

Subcutaneous ICDs

Totally subcutaneous ICDs (S-ICDs) are intended as a less invasive alternative to the conventional transvenous ICD. Therefore, 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 Trials

Published evidence for S-ICD is limited to a few nonrandomized case series. The data from case series is considered unreliable due to methodological limitations such as the lack of randomized patient selection, small sample size, and short-term study duration. These limitations also apply to the two case series that compared S-ICD with transvenous ICD. These comparison studies reported the following results:

- 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.[23] 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 ($p<0.001$).

- In 2013, Kobe et al prospectively followed 69 patients who received S-ICD.[24] These were compared with a group of 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.

Adverse Effects

Reported adverse effects of S-ICDs included the following:
- Failure to terminate arrhythmia
- Hematoma at implantation site
- Infection at implantation site
- Skin erosion at subcutaneous generator site

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.[25]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.[26] 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.

Clinical Practice Guidelines

<u>The American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) Guidelines</u>

Adult Patients

The 2012[27] ACC/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities updates the 2008[11] 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 randomized trials; and level C is when the recommendation is primarily based on expert consensus.

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 left ventricular ejection fraction (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)

Pediatric Patients

The published clinical practice guidelines concerning ICD use in pediatric populations are based on evidence from nonrandomized studies, extrapolation from adult clinical trials, and expert consensus.[11]

The 2012 ACC/AHA/HRS focused update[27] resulted in no changes to the following 2008 practice guidelines for indications for ICD use in pediatric patients:

- Class I Indications
    - Survivors of cardiac arrest, after reversible causes have been excluded (Level of evidence B)
    - Symptomatic, sustained ventricular tachycardia in association with congenital heart disease in patients who have undergone hemodynamic and electrophysiologic evaluation (Level of evidence C)
- Class IIa Indications
    - Reasonable for patients with congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias (Level of evidence B)
- Class IIb Indications
    - May be considered for patients with recurrent syncope associated with complex congenital heart disease and advanced systemic ventricular dysfunction when thorough invasive and non-invasive investigations have failed to reveal a cause (Level of evidence C)

<u>ACC/AHA Guidelines on the Diagnosis and Management of Heart Failure</u>

In April 2009, the ACC/AHA published updated guidelines on the management of chronic heart failure in adults, in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation.[28] The guidelines follow the evidence criteria listed here for ICD placement, and only Class I recommendations are listed as follows:

1. An ICD is recommended as secondary prevention to prolong survival in patients with current or prior symptoms of HF [heart failure] and reduced LVEF who have a history of cardiac arrest, ventricular fibrillation, or hemodynamically destabilizing ventricular tachycardia. (Level of Evidence: A)
2. ICD therapy is recommended for primary prevention of sudden cardiac death to reduce total mortality in patients with nonischemic dilated cardiomyopathy or ischemic heart disease at least 40 days post-MI, an LVEF less than or equal to 35%, and NYHA functional Class II or III symptoms while receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 year. (Level of Evidence: A)

American College of Cardiology Foundation/American Heart Association

In 2011, ACCF/AHA guidelines were published on the management of patients with hypertrophic cardiomyopathy.[29] These guidelines contained the following statements about the use of ICDs in patients with HCM:

- Class I Recommendations
    - 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)
    - 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
    - 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)
    - 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)
    - 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)
    - It is reasonable to recommend an ICD for high-risk children with HCM, based on unexplained syncope, massive LV hypertrophy, or family history of SCD, after taking into account the relatively high complication rate of long-term ICD implantation. (Level of Evidence: C)

- Class IIb Recommendations
    - 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)
    - 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)

Summary

ICDs in Patients with Prior Arrhythmogenic Events and Ischemic Cardiomyopathy

There is an extensive literature base on the use of implantable cardioverter defibrillators (ICDs) in patients with prior arrhythmogenic events and ischemic cardiomyopathy. Earlier trials first demonstrated a benefit in overall mortality for survivors of cardiac arrest and patients with potentially lethal cardiac arrhythmias. Multiple well-designed randomized controlled trials have also demonstrated a benefit in overall mortality for patients with ischemic cardiomyopathy and reduced ejection fraction; therefore the use of ICDs in this population is considered medically necessary.

ICD Implantation Following Acute MI

Randomized controlled trials of early implantation of implantable cardioverter defibrillators (ICDs) following acute myocardial infarction (MI) do not support a benefit for immediate ICD implantation versus delayed implantation for at least 40 days. Thus, the use of ICDs in patients with acute MI is considered investigational.

ICD for Nonischemic Dilated Cardiomyopathy (NIDCM)

For nonischemic dilated cardiomyopathy (NIDCM), there is less clinical trial evidence available, but the available evidence from a limited number of randomized controlled trials (RCTs) enrolling patients with NIDCM and from subgroup analysis of RCTs with mixed populations, supports a survival benefit for this group. There is no high-quality evidence available to determine whether early versus delayed implantation improves outcomes for patients with NIDCM, and it is not possible to determine the optimal waiting period for implantable cardioverter defibrillator (ICD) implantation following onset of NIDCM. Therefore the use of ICD implantation among patients with NIDCM is considered medically necessary, but only after a sufficient interval following inception of NIDCM.

ICD in Pediatric Patients

For pediatric patients, there is no direct evidence on the benefit of implantable cardioverter defibrillator (ICD) implantation from high-quality clinical trials. Indications for pediatric patients are based on specialty society guidelines and from specialty society clinical input, both of which extrapolate findings from adult populations to the pediatric population. This evidence base suggests that net health benefit may be experienced in some pediatric populations with history of cardiac arrest or congenital heart disease, therefore, in these subpopulations, ICD is considered medically necessary.

LMNA-related Cardiac Arrhythmia or Cardiomyopathy

Current evidence is sufficient to determine that use of implantable cardioverter defibrillators (ICDs) results in improved health outcomes compared with pacemakers or medical treatment in patients with LMNA-related cardiac arrhythmias or cardiomyopathy. Therefore, ICDs are considered medically necessary in selected patients with LMNA gene mutations.

Subcutaneous ICDs

A subcutaneous implantable cardioverter defibrillator (ICD) has been developed that does not employ transvenous leads. Current evidence is limited to small nonrandomized studies with results so far indicating that the subcutaneous ICD may approximate the performance of a transvenous ICD. However, data from case series are considered unreliable due to methodological limitations such as the lack of randomized patient selection, small sample size, and short study duration. Additional evidence from well-designed randomized controlled trials comparing subcutaneous ICDs with transvenous ICDs is needed. Due to the limited evidence, subcutaneous ICDs are considered investigational.

ICDs with ST Segment Monitoring Capability

Use of implantable cardioverter defibrillators with ST segment monitoring capability is considered investigational for the following reasons:

- No devices have received U.S. Food and Drug Administration (FDA) approval for marketing in the U.S.
- There is a lack of evidence that the addition of ST segment monitoring changes patient management or improves health outcomes.

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CODES	NUMBER	DESCRIPTION
CPT	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

CODES	NUMBER	DESCRIPTION
	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
	33249	Insertion or repositioning of electrode lead(s) for single or dual chamber pacing cardioverter-defibrillator and insertion of pulse generator
	0319T	Insertion or replacement of subcutaneous implantable defibrillator system with subcutaneous electrode
	0320T	Insertion of subcutaneous defibrillator electrode
	0321T	Insertion of subcutaneous implantable defibrillator pulse generator only with existing subcutaneous electrode
	0322T	Removal of subcutaneous implantable defibrillator pulse generator only
	0323T	Removal of subcutaneous implantable defibrillator pulse generator with replacement of subcutaneous implantable defibrillator pulse generator only
	0324T	Removal of subcutaneous defibrillator electrode
	0325T	Repositioning of subcutaneous implantable defibrillator electrode and/or pulse generator
	0326T	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)
	0327T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system
	0328T	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; implantable subcutaneous lead defibrillator system

CODES	NUMBER	DESCRIPTION
HCPCS	C1721	Cardioverter-defibrillator, dual chamber (implantable)
	C1722	Cardioverter-defibrillator, single chamber (implantable)
	C1882	Cardioverter-defibrillator, other than single or dual chamber (implantable)