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When Is It Safe Not to Re-implant An Implantable Cardioverter Defibrillator at the Time of Battery Depletion?

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Abstract/Summary

The implantable cardioverter defibrillator (ICD) is a life-saving therapy in various patient populations. Although data on the outcomes of initial ICD implants are abundant, data on ICD replacements, especially in patients with improved left ventricular function, are scarce. Therefore, it is not known when it is safe to not replace an ICD that has reached the end of battery life. In this paper, we review data on patients with primary prevention ICDs who have improvement in the left ventricular ejection fraction during follow-up and provide some guidance, based on the available evidence, related to circumstances in which replacement of an ICD may be forgone.

Keywords

sudden cardiac death; implantable cardioverter defibrillator; cardiac resynchronization therapy; left ventricular ejection fraction recovery

Several randomized clinical trials have demonstrated the efficacy of the implantable cardioverter defibrillator (ICD) in reducing sudden cardiac death and all-cause mortality in survivors of cardiac arrest, patients with sustained ventricular tachycardia and structural heart disease, and patients with significant systolic dysfunction.^{1–7} This robust evidence of the survival benefit of ICDs has not only informed professional guidelines,⁸ but it has transformed clinical practice with about 100,000 new ICDs being implanted in patients in the United States annually.⁹ The continued use of primary prevention ICDs in clinical practice has been further supported by analyses of the National Cardiovascular Data Registry ICD Registry.^{10,11}

Current guidelines provide recommendations regarding when to implant a primary prevention or a secondary prevention ICD in a given patient.⁸ However, guidance on when it is safe not to replace an ICD is missing from these guidelines. In fact, this issue was identified by the most recent guidelines that were published in 2012 as a gap in knowledge in need of further research. Specifically, the guidelines state that: “Indicators should be

identified that provide direction about when it is safe to not replace an ICD that has reached the end of its effective battery life.”⁸

The appropriate use criteria document generated by the Heart Rhythm Society (HRS) and the American College of Cardiology (ACC) also reflects the current uncertainty regarding the best treatment strategy for older patients whose ICD reaches end of life in the setting of an improved left ventricular ejection fraction (LVEF) and no prior ICD shocks for life-threatening arrhythmias. The document states that among patients with improved heart function and no prior ICD shocks, generator replacement may be “at times an appropriate option.”¹² This recommendation was supported mainly by expert opinion and not by high-quality studies. In this article, we will review guideline recommendations regarding ICDs, summarize published data on the outcomes of patients with primary prevention ICDs with or without cardiac resynchronization therapy (CRT) who have improvement in the left ventricular (LV) function, provide some guidance regarding situations in which it may be safe to not replace an ICD, and identify gaps in the existing evidence on this topic that should be addressed by future research.

Current Indications for ICDs:

The most recent guideline document on device-based therapy of cardiac rhythm abnormalities lists the following class I indications for the ICD:⁸

1. “Survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable sustained ventricular tachycardia (VT) after evaluation to define the cause of the event and to exclude any completely reversible causes.
2. Patients with structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable.
3. Patients with syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or ventricular fibrillation induced at electrophysiological study.
4. Patients with LV dysfunction due to prior myocardial infarction (MI), 40 days post-MI, LVEF < 35%, New York Heart Association (NYHA) class II or III.
5. Patients with non-ischemic cardiomyopathy and LVEF < 35%, NYHA class II or III
6. Patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF less than or equal to 30%, and are in NYHA functional Class I.
7. Patients with nonsustained VT due to prior MI, LVEF less than or equal to 40%, and inducible ventricular fibrillation or sustained VT at electrophysiological study.”⁸

Multiple class IIa indications for ICDs are also listed in the guideline document. These class IIa indications involve milder presentations of class I scenarios such as unexplained syncope with significant systolic dysfunction due to non-ischemic cardiomyopathy or sustained VT in patients with normal or near-normal ventricular function.⁸ All recommendations on ICDs

stipulate that patients be on optimal medical therapy and have a reasonable expectation of survival for more than 1 year.⁸ As stated previously, the guidelines do not offer any guidance on when not to re-implant an ICD.

Data on ICDs:

During an ICD generator's typical lifetime of approximately 7–10 years, about 65% of patients do not receive ICD shocks and up to 45% of patients have a substantial improvement in their LVEF to > 35%, such that they would no longer meet accepted indications for a new ICD.^{13,14} In a study of 195 patients, 50 (25.6%) had 10% improvement in LVEF reaching a median LVEF during follow-up of 41% (25th, 75th percentiles 37%, 49%).¹⁵ Studies have shown that LVEF improvement is associated with a significant long-term reduction in heart failure hospitalizations, ICD shocks, and death.^{13,16–18} Among patients with ICDs, one of the strongest predictors of ICD shocks is a prior heart failure hospitalization.¹⁹ The close correlation between the LVEF, worsening heart failure, and the risk of ventricular arrhythmias has raised questions about the benefits of ICD in patients with substantial improvement in the LVEF.^{20,21}

However, a few retrospective studies with relatively small sample sizes have shown a non-trivial rate of appropriate ICD shocks even in patients with significant LVEF improvement.^{22–24} In a secondary analysis of the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE), patients whose LVEF improved had lower mortality risk compared with patients whose LVEF decreased, but appropriate shocks did not significantly correlate with LVEF improvement during follow-up.²² Another study of 91 patients with primary prevention ICDs found that at generator replacement, 25 patients (27%) had improved LVEF. During a mean follow-up of 6 years, 9 patients (36%) with improved LVEF versus 19 (29%) with unchanged LVEF had appropriate ICD shocks.²³ In an analysis of 154 primary prevention ICD patients needing replacement because of battery depletion, 114 (74%) patients had not received appropriate ICD therapy. Following ICD generator replacement, the 3-year incidence of appropriate therapy in these patients was 14%; however, this study did not include information on the incidence of LVEF improvement.²⁴ In a similar study, 275 of 403 patients (68%) needing a primary prevention ICD replacement had not received an appropriate therapy from the initial device. After ICD generator replacement, the 3-year risk of appropriate ICD therapy was 13.7%, but no information on follow-up LVEF was provided.²⁵ So, based on these data, it seems appropriate to replace the ICD in patients with a primary prevention ICD who continue to meet the guideline recommendations at the time of device replacement.

Given the conflicting data on the outcomes of ICD patients with an improved LVEF and the paucity of data from prospective studies on the best management practices, it is not known whether ICD generator replacement should be performed in patients who no longer meet current indications for an ICD (due to an improved LVEF to > 35% and in the absence of prior ICD shocks).^{20,26} This uncertainty is amplified in patients 65 years of age in whom the burden of comorbid diseases and competing modes of death reduce ICD benefit.^{26,27} Although many studies have defined the risks associated with ICD generator replacement,

^{28,29} there are currently no studies that have examined whether or not this invasive procedure leads to any benefit among these lower-risk patients.

The critical importance of understanding the best care strategy for individuals who no longer meet current indications for an ICD (due to an improved LVEF > 35% and absence of prior ICD shocks) has been emphasized by patients, care partners, physicians, and professional organizations. In early 2015, as part of its prioritization process, the Patient Centered Outcomes Research Institute (PCORI) tasked the Duke University Evidence Synthesis Group (ESG) to work with diverse stakeholders to identify and prioritize the future research that is most needed by patients and other decision makers on the topic of ICDs in older patients. The results identified “clinical effectiveness and safety of ICD replacements in older patients who have not had an appropriate shock or those with improved LVEF” as a key research priority for PCORI.²⁶

ICD generator replacement is associated with a non-trivial risk of complications; within 6 months after the procedure, the risk of major complications is 4% and the risk of minor complications is 7.4%.²⁸ Major complications associated with ICD generator replacement include lead dislodgement or damage, device infection requiring removal of the entire ICD system, significant bleeding requiring ICD pocket evacuation, and prolonged hospitalization.²⁸ Minor complications include nerve injury, minor bleeding, skin infection, and pain. The risk of device infection is particularly troubling as it does not only appear to be increasing, but it generally requires removal of the whole ICD system. In a study of the National Hospital Discharge Survey database from 1996 through 2006, the risk of device infection was noted to have increased from 2004 to 2006 by 57%.³⁰ Factors that could account for this rise in device infection included an increase in the rate of comorbid illnesses like end-organ failure and diabetes mellitus and an increase in the use of CRT devices.³⁰ Removal of the entire ICD system (generator and leads) is associated with substantial risks including cardiac perforation with or without tamponade, vascular damage, and even death.^{31,32}

Therefore, until more data become available, the following algorithm can be used to make decisions regarding ICD generator replacements:

In reviewing this algorithm, it is important to note that the LVEF measurement is subjective with an inter- and intra-observer variability that approaches 5–8%, so it may be better to use a cutoff for the improved LVEF at battery depletion of > 40% or > 45% to allow for that variability. Also, although the annual risk of receiving ICD therapy among patients with LVEF improvement is relatively small, low to moderate quality studies have shown that over 5 years, >10% (sometimes > 20%) of patients end up receiving an appropriate therapy. This information should be considered and shared with the patient during clinical decision making. Finally, if ICD replacement is forgone, it may be important to obtain periodic follow-up assessments of the LVEF to look for worsening to 35% at which point replacement of the ICD may be appropriate.

Data on Cardiac Resynchronization Therapy-Defibrillator

CRT has become one of the mainstay therapies in patients with heart failure with a reduced LVEF ($< 35\%$) who have a wide QRS and symptomatic heart failure despite optimal medical therapy.⁸ Many studies have shown that this therapy improves patients' survival, quality of life, and functional status and reduces heart failure hospitalization.^{33–37} CRT devices are either pacemakers (CRT-P) or defibrillators (CRT-D). Both types of devices resynchronize the heart through biventricular pacing; CRT-D can also deliver high-energy shocks or anti-tachycardia pacing to terminate life-threatening ventricular arrhythmias. Patients who receive a primary prevention CRT-D as their initial device may have significant improvement in their LVEF due to CRT and as such their risk of ventricular arrhythmias may decrease substantially. In such patients, when the battery reaches end of life, it is not known whether a CRT-P may suffice. The HRS/ACC Appropriate Use Criteria document considered these types of scenarios and determined that it may be appropriate to replace a CRT-D with a CRT-P device in patients who received a CRT-D device when the LVEF $< 35\%$ and the LVEF at end of battery life is $< 36\%$.¹²

A few studies have reported on the risk of appropriate ICD shocks from CRT-Ds in patients with an improved LVEF. In a landmark analysis of 270 patients with post-CRT-D LVEF assessment and no ICD therapy within 1 year of device implantation, the 2-year risk of appropriate ICD therapy was 3.0%, 2.1%, and 1.5% for post-CRT-D LVEF of 45%, 50% and 55%, respectively. This study concluded that when the LVEF near normalizes to $> 45\%$, the incidence of ICD therapies for ventricular arrhythmias decreases appreciably.³⁸ In another study of 270 patients, the LVEF improved to $> 35\%$ in 21% of patients during a follow-up period of 12 months. Patients with an LVEF improvement to $> 35\%$ received fewer ICD therapies during follow-up than those who did not (23 vs. 38%; P-value 0.03). Limiting the analysis to patients with a primary prevention ICD showed that the rate of ICD therapies was 31% in patients with no LVEF improvement versus 6% in patients with an LVEF improvement to $> 35\%$.³⁹

Another study reported on the risk of appropriate ICD shocks in 110 patients with CRT-D who had an absolute increase in the LVEF of $\geq 10\%$, a decrease in LV end-systolic volume of $\geq 30\%$, or a decrease in LV end-diastolic volume of $\geq 20\%$. They found these 3 groups of patients received ICD shocks ((3-year risk: 64% vs 82% for LVEF $\geq 10\%$; 63% vs 92% for end-systolic volume $\geq 30\%$; and 62% vs 94% for end-diastolic volume $\geq 20\%$; all $p < 0.001$) during a mean follow-up duration of 25 months; however, this study was limited by the relatively small sample size and short follow-up.⁴⁰ In another study of 142 patients with a primary prevention CRT-D and a baseline LVEF $< 35\%$, 42 had an improvement in the LVEF to $> 35\%$ over a median follow-up of 3 years. None of these 42 patients had appropriate ICD therapies during follow-up.⁴⁰

A secondary analysis of the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT) trial focused on 752 patients who survived and had echocardiographic data at enrollment and at 12 months. During an average follow-up period of 2.2 years, 7.3% patients had LVEF normalization. The risk of ventricular arrhythmias was significantly lower in patients with LVEF $> 50\%$ (hazard ratio

[HR], 0.24; 95% confidence interval [CI], 0.07–0.82; $p=0.023$) and LVEF of 36% to 50% (HR, 0.44; 95% CI, 0.28–0.68; $p<0.001$). Because the risk of inappropriate ICD therapy was non-trivial, the authors concluded that patients with LVEF improvement could be considered for downgrade from CRT-D to CRT-P when the battery reaches end of life if no ventricular arrhythmias had occurred.⁴¹

Finally, a meta-analysis was conducted to determine the association between LVEF recovery following CRT and the risk of appropriate ICD therapy.⁴³ Six retrospective cohort studies were included ($n=1740$). The risk of appropriate ICD therapy was significantly lower in patients with post-CRT LVEF $\geq 35\%$ (5.5/100 person-years) than patients with post-CRT LVEF $<35\%$ [incidence rate difference $-6.5/100$ person-years, 95% confidence interval (95% CI): -8.8 to -4.2 , $p=0.001$]. Focusing the analysis on patients with a post-CRT LVEF of $\geq 45\%$ showed a lower risk of ICD therapy (2.3/100 person-years) compared with patients without such recovery ($-5.8/100$ person-years, 95% CI: -7.6 to 24.0 , $p=0.001$). Patients with a primary prevention ICD had very low rates of ICD therapy (0.4 to 0.8/100-person years) irrespective of LVEF recovery. The investigators concluded that LVEF recovery post-CRT is associated with significantly reduced appropriate ICD therapy, and this risk is lowest in patients with improvement of LVEF $\geq 45\%$ and those with a primary prevention indication.⁴³

Based on the aforementioned studies, it is not known how to best manage patients with a CRT-D device with no prior ICD therapies who have significant improvement in the LVEF at the time of battery depletion. Therefore, randomized clinical trials of CRT-P vs. CRT-D especially at the time of device replacement are needed. Until such trials are completed, the following algorithm can be used to make decisions regarding CRT-D generator replacements:

Conclusions:

A large number of patients with a primary prevention ICD or a CRT-D have significant improvement in their left ventricular function during follow-up. Patients with an ICD and improved LVEF to $> 45\%$ appear to be at a low risk of ventricular arrhythmias; however, there are no data from prospective studies on whether it is safe to not replace the ICD in such patients. In patients with a CRT-D who have significant improvement in their left ventricular function, evidence from retrospective studies suggests that the risk of future ventricular arrhythmias is very low in patients with a primary prevention indication whose LVEF improves to $\geq 45\%$ with CRT. However, there are no data on whether replacing the CRT-D with a CRT-P in such patients is safe. It is noteworthy that the absolute LVEF value during follow-up may not be enough in assessing the risk of ventricular arrhythmias; it is possible that the magnitude of improvement is more important than whether the LVEF is $<$ or $> 35\%$. Future studies should look at the predictive power of the LVEF as a continuous variable. In addition, future randomized clinical trials should compare the outcomes of ICD replacement versus not and CRT-D versus CRT-P at the time of battery depletion. Until data from clinical trials are available to guide clinical recommendations, shared decision making is essential taking into account the uncertainties in the data and the known pros and cons of replacing versus not replacing the ICD.

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Key points

1. Available data suggest that up to 45% of recipients of primary prevention ICDs have significant improvement in their left ventricular function during follow-up. Although prospective data on the outcomes of patients with a primary prevention ICD and substantial improvement in left ventricular function are scarce, such patients appear to be at a low risk of ventricular arrhythmias.
2. Prospective data are limited on the outcomes of patients with a cardiac resynchronization therapy defibrillator (CRT-D) who have significant improvement in their left ventricular function; however, the cumulative evidence from retrospective studies suggests that the risk of future ventricular arrhythmias is very low in patients with a primary prevention indication whose left ventricular ejection fraction (LVEF) improves to $\geq 45\%$ with CRT.
3. It is not known when it is safe to not re-implant an ICD in patients with a primary prevention ICD with or without CRT.
4. Until more data are available, the 2 situations in which it may be safe not to re-implant an ICD are: (1) patients with a primary prevention ICD who have significant improvement in left ventricular function (LVEF $\geq 45\%$), no prior ICD therapies and no bradycardia pacing indication and (2) patients with a primary prevention CRT-D who have an improvement of the LVEF to $\geq 45\%$ with CRT. If ICD replacement is forgone, it may be important to periodically assess the LVEF to look for worsening to $\leq 35\%$ at which point replacement of the ICD may be appropriate.
5. Randomized clinical trials are needed on ICD replacement versus not and on CRT-D versus CRT-P at the time of battery depletion.

Fig. 1. ICD generator replacement decision algorithm. ^a The LVEF measurement is subjective and the variability may be up to 8%, so it may be better to use a cutoff of 40% or 45% to allow for that variability.

* LVEF cutoff of 45% was used based on data from Chatterjee et al (Reference 43)

Fig. 2.

CRT-D generator replacement decision algorithm. ^a LVEF cutoff of 45% was used based on data from Chatterjee et al.⁴³

(Data from Chatterjee NA, Roka A, Lubitz SA, et al. Reduced appropriate implantable cardioverter-defibrillator therapy after cardiac resynchronization therapy-induced left ventricular function recovery: a meta-analysis and systematic review. *Eur Heart J* 2015;36(41):2780–9.)