

# To Replace or Not to Replace: What to do with the implantable cardioverter-defibrillator generator when the left ventricular function has improved

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## Abstract

This editorial reviews the data to guide the discussion on whether or not to replace implantable cardioverter-defibrillator generator when the left ventricular ejection fraction has improved.

## To Replace or Not to Replace: What to do with the implantable cardioverter-defibrillator generator when the left ventricular function has improved

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A 70-year-old man with a single-chamber implantable cardioverter-defibrillator (ICD) presented because his ICD was nearing the end of battery life. The ICD, implanted 8 years ago for primary prevention of sudden cardiac death (SCD), has not delivered any appropriate therapies. His left ventricular ejection fraction (EF), which was 30% at the time of ICD implantation, has improved to 45% since then. Is the ICD generator replacement justified?

Approximately 30,000 ICD generator replacement procedures are performed in the US annually for nearing the end of battery life (ERI), constituting 28% of all ICD procedures.<sup>1,2</sup> While it is common practice to routinely replace ICDs that reach ERI, several factors may limit or accentuate their future potential benefit: First, patients presenting for ICD generator replacement are older and have more comorbidities than those having initial ICD implant, increasing the competing risks of death from non-cardiovascular causes. Indeed, 10% of the patients who underwent ICD replacement die after one year and up to 50% die after five years from causes that the ICD therapies cannot treat.<sup>1</sup> Second, they may have had appropriate ICD therapies for ventricular tachycardia or ventricular fibrillation (VT/VF), increasing the likelihood of future VT/VF. The patients who had appropriate ICD therapy are usually considered to have a secondary prevention indication for ICD from that point on. Third, they may have had an improvement in left ventricular ejection fraction (EF) since ICD implantation, reducing the likelihood of future VT/VF.<sup>3,4</sup>

Left ventricular EF is the cornerstone of the criteria used in the decision for ICD implantation for primary prevention of SCD. Professional society practice guideline statements recommend ICD implantation in patients with EF  $\geq 35\%$  and mild to moderate heart failure symptoms while taking optimal medical therapy. However, 30-40% of the patients with a primary-prevention ICD experience an improvement in their EF to the extent that they are no longer eligible for ICD when they present for generator replacement.<sup>3,4</sup> Patients who experience an improvement in EF are younger, more likely to be women, more likely to be taking heart failure medications, and more likely to have non-ischemic cardiomyopathy.<sup>3,4</sup> While there is a close audit of indications at initial ICD implantation routine re-assessment of ICD indications is not mandated when these patients present for ICD generator replacement. Identifying the patients who are least likely to benefit from continued ICD therapy may significantly reduce procedure-related risks and cost, by avoiding unnecessary ICD generator replacement.

In this issue of the journal, Chang et al. present the results of a retrospective cohort study evaluating the risk of appropriate ICD therapies in 423 patients who underwent ICD generator replacement.<sup>5</sup> Notably, all ICDs were implanted for primary prevention of SCD and no patient had received appropriate ICD therapies in the past. The analyses were adjusted for competing risk of death. At the time of generator replacement 38% of the patients had EF  $\geq 35\%$ . The risk of appropriate ICD therapy was 2.13 times higher in patients whose EF remained  $<35\%$  in comparison to those with EF improvement to  $\geq 35\%$  (Fine-Gray adjusted 5-year event rates 25.0% vs. 12.7%, respectively;  $p=0.002$ ). While the EF was a poor predictor of future appropriate ICD therapy (c-index 0.62), risk stratification was better at EF cutoff 45%. Patients whose EF was  $<45\%$  had a 4.42 times higher risk of appropriate ICD therapy compared to those with EF  $\geq 45\%$  (Fine-Gray adjusted 5-year event rates 25.1% vs. 6.4%, respectively;  $p<0.001$ ). These associations were also observed in subgroups with or without ischemic cardiomyopathy and in those with or without cardiac resynchronization therapy.

These results are in line with prior cohort studies. In a retrospective cohort study conducted in a similar cohort almost a decade earlier, Madhavan et al. reported 12% versus 5% annual risk of appropriate ICD therapy after generator replacement in patients with EF  $<35\%$  vs.  $\geq 35\%$ , respectively.<sup>6</sup> In other cohort studies improvement in EF was associated with a significant reduction in the risk of appropriate ICD therapy, but was not eliminated, ranging from 2.8% to 5% per year.<sup>3,4</sup> The persisting risk of arrhythmias, observed in some patients despite improvement in EF may be partly explained by the presence of a fixed substrate for ventricular arrhythmias (e.g., fibrosis, myocardial scar, heterogeneous repolarization) that does not resolve even when EF improves. However, none of the prior studies assessed the risk of ICD therapy using an EF cutoff 45% and none provided event rates adjusted for the competing risk of mortality. As such, the study by Chang et al.<sup>5</sup> advances the field significantly.

Do ICDs save lives if the EF has improved to  $\geq 35\%$ ? In a secondary analysis of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Adabag et al. found that both patients with EF improvement to  $\geq 35\%$  and those whose EF remained  $<35\%$  accrued a similar relative risk reduction in mortality with ICD compared to placebo (hazard ratio 0.6 in both groups), suggesting that ICD generator replacement may reduce mortality even after EF has improved to  $\geq 35\%$ .<sup>7</sup> However, post-hoc analyses of old randomized trial data cannot replace the need for prospective randomized controlled trials.

At the time ICD reaches ERI, patients and their physicians may use varying criteria to decide whether to undergo/perform generator replacement, considering the patient's age, comorbidities, and competing risks of death. While the risk of future VT/VF is never zero, each individual patient may have their own threshold of risk below which they would choose to forgo generator replacement. Ideally, the possibility of not replacing the ICD generator when the device reaches ERI should be introduced at the initial implantation.

Patients who present for ICD generator replacement should be re-evaluated for the appropriateness of continued ICD therapy. The evaluation should exclude any potential contraindications, such as advanced malignancy or dementia, that may have developed since the initial implant. A validated mortality risk prediction score may facilitate the discussion by providing an objective estimate of the patient's mortality risk.<sup>8,9</sup> A frank discussion to learn the patient's wishes for end-of-life care in relation to continued ICD therapy is of

utmost importance to help guide the decision and to clarify potential misconceptions. Older patients who have developed competing risks of death due to new comorbidities (e.g., renal failure) or those with frailty, disability or cognitive dysfunction should have an opportunity to reevaluate continued ICD therapy with an extensive discussion of goals of care.<sup>10</sup>

We propose an algorithm to guide ICD generator replacement decision (Figure). At the time of ERI, we recommend replacement of the generator if the original indication for ICD was secondary prevention of SCD. The risk of appropriate ICD therapy is higher (10%/year versus 5%/year) if the ICD was implanted for secondary prevention of SCD. We also recommend generator replacement if there was an appropriate ICD therapy (shock or anti-tachycardia pacing) in the past. Patients whose EF remains  $\geq 35\%$  continue to be at SCD risk and should undergo generator replacement if they wish to continue ICD therapy. On the other hand, patients with EF improvement deserve a fair discussion of whether the SCD risk warrants continuation of ICD therapy. Some patients with normalized or close-to-normal EF may not have sufficiently high risk of VT/VF to benefit from continued ICD therapy. Patients with non-ischemic cardiomyopathy have a lower risk of SCD and may not benefit from ongoing ICD therapy if EF has improved.<sup>11</sup> On the other hand, patients with a prior myocardial scar may continue to benefit from ICD even if their EF is better.

Despite the informative results from the present and prior studies, some questions remain regarding the management of patients with improved EF presenting for ICD generator replacement. Does the use of modern-day heart failure therapy, specifically sacubitril/valsartan and sodium-glucose transporter-2 inhibitors, confer even lower risk of ICD therapy? The field continues to evolve. In this regard, data from the study by Chang et al.<sup>5</sup> will be very valuable, to facilitate the discussion between patients and their physicians.

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## Figure Legends

**Figure 1.** Recommended algorithm for the management of patients presenting for ICD generator replacement

## Hosted file

Figure algorithm.docx available at <https://authorea.com/users/341979/articles/641101-to-replace-or-not-to-replace-what-to-do-with-the-implantable-cardioverter-defibrillator-generator-when-the-left-ventricular-function-has-improved>