

## Paradox of Appropriate Implantable Cardioverter-Defibrillator Therapy: Saving Lives But Revealing an Increased Mortality Risk

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At one time, implantation of an implantable cardioverter-defibrillator (ICD) was reserved for those patients who survived sudden cardiac death (SCD) from ventricular arrhythmia and had a secondary-prevention-only indication. However, along with improvements in device technology and the implant procedure, the indications for offering an ICD broadened to include those at the highest risk of SCD from ventricular arrhythmia for primary prevention. Patients receiving an ICD for primary prevention have a lower rate of appropriate ICD therapy but more comorbidities compared with those who receive an ICD after surviving SCD. In general, primary-prevention ICD patients live longer than those with a secondary-prevention indication. However, once a primary-prevention patient receives appropriate therapy and thus is declared a secondary-prevention patient, are the improved patient characteristics still associated with reduced mortality?

In the current issue of *JAHA*, Almeahadi and colleagues present an interesting analysis of the implications of ICD shock or antitachycardia pacing (ATP) in a large cohort of patients who received ICDs for primary- and secondary-prevention indications.<sup>1</sup> Several important findings resulted from this analysis. First, patients who receive any appropriate ICD therapy, either shock or ATP, have increased mortality no matter what the initial indication. Second, patients who received an ICD for a secondary-prevention indication have higher risk of subsequent ICD therapy compared with those with a primary-prevention ICD. The most important finding, however, was that the risk of subsequent death was similar in both groups (primary versus secondary prevention) once they received any ICD therapy. This finding was surprising because

patients in the primary-prevention ICD group were older and had more comorbidities, with higher incidence of diabetes mellitus and hypertension and more advanced heart failure. Given that the secondary-indication ICD group was “healthier,” this finding suggests that a higher burden of ventricular arrhythmias was a risk factor sufficient to confer increased mortality. Furthermore, mortality risk was increased in both groups regardless of whether the patient received ATP or an ICD shock, in contrast to the MADIT-RIT (Multicenter Automatic Defibrillator Implantation Trial–Reduce Inappropriate Therapy) trial.<sup>2</sup>

This analysis has numerous strengths including the large number of patients in this single Canadian province registry who had longer follow-up than many other trials and databases. In addition, the data had significant granularity to the extent that patients were excluded if covariate data were missing.

The value of this analysis is the demonstration that once patients with ICDs receive an appropriate shock or ATP, their risk of mortality increases. This effect for patients with secondary-prevention ICDs had not been demonstrated previously. Previous data from the secondary-prevention AVID (Antiarrhythmics Versus Implantable Defibrillators) trial did not show a difference in mortality with any ICD therapy.<sup>3,4</sup> The difference in the 2 trials may be due to the greater number of patients included in the analysis by Almeahadi et al.

Based on the results, the authors conclude that once patients with an ICD develop ventricular arrhythmias, an aggressive effort needs to be directed at suppressing these arrhythmias to improve survival. Although this conclusion may hold water, several limitations of the analysis include the fact that the reasons for death were not separated into those caused by arrhythmic death or progressive heart failure. Furthermore, the analysis was based on outcomes after the first ICD therapy, and we do not know what happened to patients subsequently, for example, whether there were more ICD shocks or whether other therapies were initiated to decrease further arrhythmias, such as ablation or antiarrhythmic medications.

Despite these limitations, many studies suggest that early strategies to suppress ventricular arrhythmias may improve survival. Studies such as SMASH VT (Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia) and VTACH (Ventricular Tachycardia Ablation in Coronary Heart

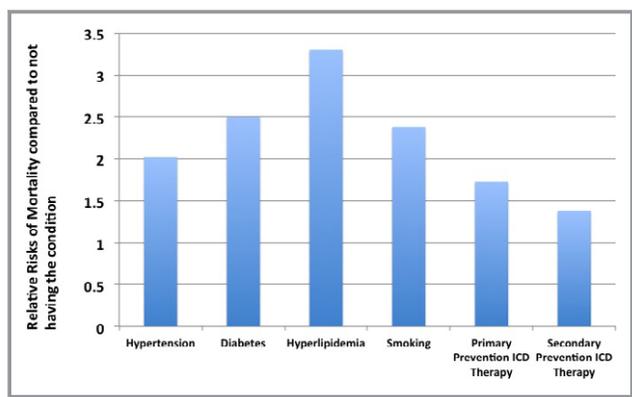
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**Figure.** Relative risks of mortality for common cardiovascular risk factors compared with increased risks of mortality with ICD therapies. ICD indicates implantable cardioverter-defibrillator.

Disease) suggested that an early, even prophylactic, ablation strategy decreased future ventricular arrhythmias.<sup>5,6</sup> More recent data show that successful ablation for ventricular tachycardia is associated with improved survival compared with unsuccessful ablation.<sup>7–9</sup> These studies are relevant to the current analysis because the majority of the patients had ischemic heart disease, although there have been similar results for patients with nonischemic cardiomyopathy.<sup>10</sup> With advances in ablation technology, such as catheters that measure contact force, further experience with epicardial ablation, and better appreciation of the variation in the ventricular substrate, ablation may be a means to improve outcomes once patients have been declared as having a higher risk of ventricular arrhythmias.

Although multiple studies have described the association of improved mortality with successful management of ventricular tachycardia, this implied causation has not been proven in a randomized trial. In addition, it is not clear how these data fit in with the multiple studies suggesting that longer detection times to reduce ICD shocks may improve outcomes.<sup>2,11</sup> The fact that patients who had ATP as their initial therapy had an increased risk of mortality similar to those who received a shock suggests that any ventricular arrhythmias may identify a higher risk patient. That said, it is unclear what subsequent therapies may have been used in patients with initial ATP. It is also not clear whether prevention of subsequent appropriate ICD therapy—although certainly a desirable clinical outcome—will result in reduced mortality risk.

The authors have uncovered an important finding in this retrospective analysis of registry data highlighting that therapy for ventricular arrhythmias represents an important risk factor for increased mortality in ICD patients. Consequently, there is a paradox in appropriate ICD therapy: It rescues a patient from a lethal ventricular arrhythmia but, at the same time, reveals a subsequent risk of mortality.

Although it remains unknown whether this mortality risk factor is modifiable with effective ablation, we know that ablation for ventricular tachycardia has been shown to effectively suppress ventricular arrhythmias and to prevent recurrent ICD therapy; therefore, it is our opinion that catheter ablation should become a more routine aspect of the treatment algorithm for these patients. Our goal should be to treat and reverse a mortality risk factor soon after it is first recognized, regardless of whether it is hypercholesterolemia,<sup>12</sup> hypertension,<sup>13</sup> diabetes mellitus,<sup>12</sup> tobacco use,<sup>12</sup> or, in this case, ventricular arrhythmias (Figure).

## Disclosures

None.

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