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THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

Implantable Cardioverter-Defibrillators at End of Battery Life

Opportunities for Risk (Re)-Stratification in ICD Recipients

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ABSTRACT

Although implantable cardioverter-defibrillators (ICDs) are frequently viewed as a lifelong commitment in that patients are routinely scheduled for generator exchange (GE) at end of battery life, several considerations should prompt a reevaluation of risks and benefits before GE. Compared with initial ICD implant, patients receiving replacement devices are older, and have more comorbidities and shorter life expectancy, all of which may limit the benefit of ICD therapy following GE. Additionally, GE is associated with significant complications, including infection, which may increase the risk of mortality. In this paper, we review recent data regarding opportunities for risk stratification before GE, with a particular focus on those with improved left ventricular function and those who have not experienced ICD therapies during the first battery life. We also provide a broader perspective on ICD therapy, focusing on how decisions regarding GE may affect goals of care at the end of life. (J Am Coll Cardiol 2016;67:435–44) © 2016 by the American College of Cardiology Foundation.

Implantable cardioverter-defibrillator (ICD) therapy is associated with significant reductions in all-cause mortality among appropriately selected patients at heightened risk of sudden cardiac death (SCD) resulting from ventricular arrhythmia (VA). The decision to implant an ICD is complex, taking into account the risk of SCD/VA, along with noncardiac comorbidities and overall life expectancy. However, several large, randomized clinical trials have been performed to assess the efficacy of ICD implantation in both primary and secondary prevention of SCD/VA. These studies serve as the foundation for the American College of Cardiology Foundation/American Heart Association/Heart Rhythm Society guidelines on ICD implantation (1) and, in conjunction with large registry studies assessing the safety and risks associated with ICD implantation (2,3), provide the basis for patients and providers to have an informed discussion about the benefits and risks of ICD implantation.

More than 100,000 ICDs are implanted annually in the United States, of which approximately three-quarters are new device implants and about one-quarter are generator exchanges (GEs) for end of battery life (4). Whereas a robust body of literature exists to support informed decision making at the time of initial ICD implant, there is a relative paucity of data to support decision making at the end of battery life. ICD therapy is frequently viewed as a lifelong commitment in that patients are scheduled for GE as a matter of course at the end of battery life. However, several important considerations should prompt a reevaluation of risks and benefits to ongoing ICD therapy before GE. First, compared with patients undergoing initial ICD implantation, those receiving replacement devices are older, have more

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CRT-D = cardiac resynchronization therapy-defibrillator

CRT-P = cardiac resynchronization therapy-pacemaker

GE = generator exchange

ICD = implantable cardioverter-defibrillator

LV = left ventricular

LVEF = left ventricular ejection fraction

SCD = sudden cardiac death

VA = ventricular arrhythmia

comorbidities, and have shorter life expectancy (5,6). This raises the possibility that, as competing risks of nonarrhythmic death accrue, the potential benefit of ICD therapy may be diminished among those undergoing GE compared with those undergoing initial implant. Additionally, although GE is generally considered a relatively straightforward procedure, elective ICD GE is associated with a major complication rate of approximately 4% (7), and the occurrence of major complications in this setting may be associated with an increased risk for mortality (8). In light of these considerations, the risk/benefit ratio of elective GE may be very different than that at the time of initial ICD implant. However, there is a paucity of data on outcomes and benefits to ongoing ICD therapy after GE, which significantly limits the ability of patients and providers to have an informed discussion.

OPPORTUNITIES FOR RISK (RE)-STRATIFICATION AT THE TIME OF GE

IMPROVED VERSUS PERSISTENTLY IMPAIRED LEFT VENTRICULAR SYSTOLIC FUNCTION. In this country, most ICDs are implanted for primary prevention, that is, in patients with impaired left ventricular ejection fraction (LVEF), but without a history of documented SCD/VA. Therefore, the mean LVEF at the time of initial ICD implant (n = 359,993) for all devices implanted between 2005 and 2010 in the National Cardiovascular Data Registry was 27.7 ± 10.8% (5). In contrast, among patients in the same registry undergoing ICD GE (n = 103,985), mean LVEF was significantly higher, at 32.6 ± 13.7%. This finding highlights that some patients who undergo initial ICD implant for impaired LVEF (i.e., ≤35%) (1) may have improvement in ventricular function between the time of initial implant and GE. There is a well-established relationship between lower LVEF and higher risk of SCD/VA, and the seminal trials establishing the efficacy of primary prevention ICD therapy (9,10) were designed, in part, on the basis of this relationship. Therefore, it is conceivable that an improvement in LVEF between initial implant and GE may alter the risk of SCD/VA, such that the risk of arrhythmic death is no longer sufficiently high to warrant ongoing ICD therapy.

Several studies have looked at outcomes after GE as a function of improvement in LVEF. In a recent study in a Veterans Affairs cohort of 231 patients undergoing GE who were initially implanted for primary prevention, ongoing ICD therapy was considered no longer indicated at the time of GE in 59 patients (26%) on the basis of LVEF improvement to ≥40% and never having received appropriate ICD therapy during the first battery life (i.e., an "uneventful" first battery life) (11). Mean LVEF at the time of GE among those in whom ICD therapy was considered no longer indicated was 49 ± 9% versus 25 ± 11% among those with persistently impaired LV function. Importantly, all patients in this cohort underwent GE. During a mean follow-up of 3.5 ± 2.0 years after GE, the incidence of appropriate ICD therapy among those in whom ICD therapy was considered no longer indicated was 2.8%/person-year, compared with 10.7%/person-year in those in whom ongoing ICD therapy was considered indicated ($p < 0.001$). These findings highlight the significantly lower risk of SCD/VA among those with improved LVEF and uneventful first battery life.

Similar findings were recently demonstrated in a follow-up study from the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) trial, in which patients who were randomized in the initial study to CRT-defibrillator (CRT-D) and had paired echocardiograms at baseline and at 12 months (n = 752) were evaluated to assess the impact of improvement in LV function on subsequent ICD therapies (12). All patients had LVEF ≤30% at the time of initial CRT-D implant and ICDs were implanted for primary prevention. At the 12-month follow-up, patients were categorized into 3 groups: LVEF ≤35%; LVEF 36% to 50%; and LVEF >50% ("normalized" LVEF group). During a mean follow-up of 2.2 ± 0.8 years after the *initial* CRT-D implant, the primary endpoint of appropriate ICD therapy for VA ≥200 beats/min occurred in only 1 of 55 patients (2%) with normalization of LVEF; this event was treated without need for ICD shock. There were no appropriate ICD shocks among patients with normalized LVEF. In contrast, the incidence of VA ≥200 beats/min was 7% among those with LVEF 36% to 50% (n = 594) and 18% among those with LVEF ≤35% (n = 103), supporting the notion of an inverse relationship between LV function and risk of SCD/VA. Two important aspects of the MADIT-CRT substudy should be noted. First, this cohort addressed improvement in LVEF and reduction in ICD therapies during the first battery life and did not specifically address prognosis after GE. Second, this study looked only at patients who had recovery of LV function with CRT, which may be mechanistically different than spontaneous improvement in LVEF with medical therapy, as in the study by Kini et al. (11).