Risk Assessment for Defibrillator Therapy

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“The Defibrillator Surgery Often Unnecessary” and “Devices Can Interfere With Peaceful Death” were the titles of newspaper articles that Mr. Michael brought to our arrhythmia service for a second opinion regarding implantable cardioverter-defibrillator (ICD) therapy (1,2). Mr. Michael (names in this commentary are fictitious) is a 67-year-old with New York Heart Association (NYHA) functional class II congestive heart failure (CHF) symptoms. He had a myocardial infarction (MI) followed by 3-vessel coronary bypass grafting (CABG) 6 years before. Left ventricular ejection fraction (LVEF) is 27%. An electrocardiogram shows left bundle branch block. A Holter showed 334 premature ventricular complexes (PVCs) per hour and up to 5 beat runs of nonsustained ventricular tachycardia (NSVT). A test for T-wave alternans was indeterminate due to frequent PVCs (3).

The second patient, Sister Angela, is an 82-year-old retired nun referred for treatment of NYHA functional class III CHF symptoms. She has atrial fibrillation, intraventricular conduction disturbance, severe renal impairment, and a history of anterior MI. An echocardiogram showed anteroapical aneurysm and LVEF 24%. The third patient, Mr. Gianni, is a 58-year-old diabetic with NYHA functional class II CHF referred for ICD implantation. He has a history of MI and CABG 3 years before. An echocardiogram showed global hypokinesis with ejection fraction 32% and QRS duration is 98 ms. None of the patients have a history of syncope or other symptoms suggestive of a sustained ventricular tachyarrhythmia or evidence of myocardial ischemia.

The 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death recommend ICDs for each of the 3 patients at a class I level (4). However, it is up to the clinician to determine the benefits and risks of ICD therapy and to inform the patient. The evidence suggests this is rarely successful. Most ICD patients have major misconceptions, with over 50% believing that ICDs would save more than 50 lives per 100 over 5 years and more than 95% overestimating the number of lives saved compared with the results of SCD-HeFT (Sudden Cardiac Death-Heart Failure Trial) (5,6). We told our 3 patients that 64% of patients similar to them enrolled in the SCD-HeFT study survived 5 years with standard therapy but that with an ICD 71% survived (6). Inappropriate decisions for ICD replacement in response to safety advisories indicate that patients are also poorly informed about the risks of ICD therapy to the level of detail recommended (7). For each patient, we reviewed possible operative complications, device malfunctions and failures, and the pain and psychiatric problems associated with shocks. We also discussed follow-up requirements and medical, occupational, and recreational restrictions.

Mr. Michael declined ICD therapy, citing a newspaper story that many ICD recipients “may not need them” (1). We reviewed data that showed that patients like him with frequent PVCs and indeterminate T-wave alternans tests are not at low risk for arrhythmic death (8,9). A second newspaper article reported repeated shocks near the end of life (2). We reassured Mr. Michael that his risk of cardiovascular deterioration and nonarrhythmic death was not high. This was based on the finding in the SCD-HeFT study that NYHA functional class II patients had a 5-year survival that rose from 68% to 80% with an ICD (5). Furthermore, he had none of the predictors of early mortality after ICD implantation reported by Parkash et al. (10): age >80 years, history of atrial fibrillation, creatinine >1.8 mg/dl, and NYHA functional class III or IV CHF. Patients like him had a 1-year mortality of only 4%. Eventually, Mr. Michael agreed to ICD therapy because of his wife’s fear that he could drop dead at any time and that the ICD could reduce this risk by about two-thirds (11).

In contrast, Sister Angela had all 4 risk factors for early mortality in ICD recipients, indicating 1-year mortality over 30% (10). Moreover, the SCD-HeFT study showed that patients with class III CHF did not benefit from ICD implantation, and the MADIT-II (Second Multicenter Automatic Defibrillator Trial) Investigators showed that severely impaired renal function predicted high mortality unresponsive to ICD therapy (6,12). We assured Sister Angela and her family that it was reasonable to decline ICD therapy. Mr. Gianni demonstrated few of the risk factors associated with worse mortality in MADIT-II (13,14),
SCD-HeFT (6), or in the study by Parkash et al. (10). He did not wish to undergo further tests for risk assessment.

These 3 cases illustrate the importance of data to address individual circumstances beyond the general findings of randomized clinical trials and the need for an efficient risk assessment method. In this issue of the Journal, Buxton et al. (15) present a new algorithm to estimate the 2-year total and arrhythmic mortality in patients with LVEF ≤ 40% due to previous MI based on the MUSTT study. Applied to Mr. Michael, the 2-year total mortality risk is 25% and the arrhythmic death risk is 11%. These estimates are comparable to 2-year risks of total (22%) and arrhythmic death (12%) in the MADIT-II study conventional treatment group (13). If the ICD reduces arrhythmic death by 67% as in MADIT-II, then Mr. Michael’s absolute and relative mortality reduction would be 7% and 28%, respectively, by 2 years (11,13). For Sister Angela, the MUSTT algorithm 2-year all-cause and arrhythmic mortality estimates are 78% and 6%, respectively. The high nonsudden mortality is compatible with the studies discussed earlier, and the low arrhythmic risk reduces the potential impact of ICD therapy and provides a rationale for declining implantation. For Mr. Gianni, the algorithm yields a 2-year mortality risk of 10% and a malignant arrhythmia risk of 3.5%, compatible with the absence of other indicators of poor prognosis.

Despite its apparent utility, the MUSTT algorithm cannot be assumed to provide accurate risk assessment for several reasons. One is that patients encountered in practice have different demographics, clinical characteristics, and outcomes from those enrolled in clinical trials (16,17). In addition, changes in background and follow-up treatment standards since the MUSTT study was conducted should improve outcomes. Furthermore, the subgroup analysis on which the MUSTT algorithm is based may have low reliability (18). Moreover, the mathematical functions used to derive the algorithm may not adequately represent the underlying biological phenomena, and the modeled sample may have significant uncharacterized elements that affect the model but are unrelated to risk.

Potential problems also exist with specific elements of the algorithm. Nonsustained ventricular tachycardia was an entry criterion, so all of the MUSTT patients have 17 points added to the arrhythmic risk score, except those few in whom NSVT is detected 4 days to 10 days after CABG. In practice, however, the status of NSVT is often not known, and determining its presence or absence is not straightforward, because its detection depends on the frequency of NSVT episodes and the duration of monitoring. Detection during prolonged in-hospital monitoring is more likely but may be associated with a different prognosis. Inducible ventricular tachycardia, also assessed in all of the MUSTT patients, adds 8 points to total mortality and 17 points to the arrhythmic death/cardiac arrest score. In practice, however, many patients do not undergo electrophysiologic studies. Although Buxton et al. (15) stipulate that use of their model be restricted to patients with asymptomatic NSVT who have undergone programmed stimulation, this would severely reduce the utility of their algorithm. It is noteworthy that age, atrial fibrillation, and NYHA functional class contribute to total mortality, but not to arrhythmic risk, consistent with some earlier studies (10). However, it is surprising that no variable reflecting renal function was identified for the MUSTT risk estimator, because several studies have demonstrated a strong independent association with mortality. In particular, there is evidence of an association between poor renal function and ICD-unresponsive sudden death (10–12).

Before it can be considered for wider clinical use, the MUSTT algorithm must be modified to accommodate patients with unknown status of NSVT and inducible ventricular tachycardia, and the role of renal function should be addressed. The algorithm should be validated by applying it to clinically relevant test populations. It is important to recognize that prediction of sudden death and cardiac arrest does not necessarily predict ICD efficacy. Randomized clinical trials show a persistent risk of sudden death despite ICD therapy that accounts for about one-third of cardiac deaths in ICD recipients (11). Demonstration of value in predicting a survival advantage of ICD therapy would necessitate a relatively complex trial with randomization of ICD therapy based on the algorithm. However, a retrospective analysis of the algorithm in the MUSTT patients who received ICDs might provide valuable data on prediction of ICD-resistant death and appropriate ICD therapy.

As our 3 patients illustrate, available risk stratification methods lack the precision and convenience that clinicians seek and the certainty that patients crave to justify the emotional and physical consequences of ICD therapy. The algorithm developed by Buxton et al. (15) for patients with previous MI has important advantages in that it provides one-stop shopping for the full spectrum of high-risk LVEF (≤ 40%) and NYHA CHF functional class (I to III), it is easy to use, it can be repeatedly applied, and it is free. However, our enthusiasm is dampened by the failure of hundreds of risk assessment schemes developed during the half-century since Smirk (19) surmised that R-on-T PVCs predict arrhythmic death and recommended administration of quinidine to prevent it. As with any new technique, the MUSTT risk estimator cannot be recommended for use in patients until its accuracy is proved. Until then, we are pleased to try out (in monitor mode) this promising algorithm to see how it compares with our other risk-stratification tools.

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REFERENCES