EDITORIAL COMMENT

Arrhythmia Risk Prediction in Patients With Preserved Left Ventricular Function

The Final Frontier?*

Thomas Klingenheben, MD
Bonn and Frankfurt, Germany

Prognosis of patients after myocardial infarction (MI) has continuously improved over the past 2 decades. From an epidemiologic point of view, however, the absolute number of patients who will have MI is expected to increase in the future. Accordingly, sudden cardiac death after MI will continue to be a significant clinical problem, with the majority of events occurring in patients with only moderately reduced or preserved left ventricular ejection fraction (LVEF) (1). Identification of MI patients with preserved LVEF >40% at risk of dying suddenly, however, is an unresolved clinical challenge.

Primary prevention of sudden arrhythmic death by prophylactic placement of an implantable cardioverter-defibrillator (ICD) is currently restricted to selected MI patients with reduced LVEF, in whom such placement has shown to be effective (2,3). In these high-risk populations, patients with reduced LVEF, in whom such placement has been shown to be effective (2,3). In these high-risk populations, the number of ICD placements needed to prevent 1 death varies between 11 at 3 years in MADIT (Multicenter Automatic Defibrillator Implantation Trial)-II and 17 at 3 years in SCD-HeFT (Sudden Cardiac Death in HEart Failure Trial), pointing to a need for further refinement of arrhythmia risk stratification in these populations. So far, only a few electrocardiogram-based arrhythmia risk parameters, such as heart rate variability, have been implemented in interventional trials to select patients for primary preventive ICD therapy, but these parameters’ role in preventing sudden cardiac death in clinical practice remains unclear (4). Microvolt T-wave alternans (MTWA) has widely been studied as a new risk stratifier in patients with reduced left ventricular function (5,6), with a focus of the most recently published studies on patients fulfilling MADIT-II criteria (7–9). In a recent study by Chow et al. (9), for example, MTWA was measured in 768 patients with ischemic cardiomyopathy and LVEF ≤35%. A non-negative (positive or indeterminate) MTWA test was associated with a high risk of all-cause and arrhythmic mortality. Given the high negative predictive value of MTWA in these studies, “low-risk” patients with severely reduced LV function can be identified who may not benefit from ICD therapy. Microvolt T-wave alternans may thus be useful to tailor preventive ICD therapy to patients at particularly high risk, thus reducing the numbers needed to treat to prevent sudden death.

In contrast, identifying patients prone to sudden cardiac death from a population that at first glance is considered to be at low risk is even more challenging. In this issue of the Journal, Ikeda et al. (10) present the first study on the use of MTWA in a population of post-MI patients exclusively with preserved LV function (LVEF ≥40%). Also, time domain ventricular late potentials and nonsustained ventricular tachycardia during Holter recording were assessed. Nearly 99% of patients underwent coronary revascularization procedures during the acute phase of their index MI. One important finding of the present study is that LVEF was not helpful in assessing arrhythmogenic risk in patients with preserved LV function since a LVEF <45% was not associated with increased propensity to serious arrhythmic events. The incidence of a positive MTWA in the present study is 17% and thus far lower than in patients with congestive heart failure and ischemic cardiomyopathy (7). With regard to predicting the primary end point of serious arrhythmic events, defined as sudden cardiac death, cardiac arrest, or resuscitated ventricular fibrillation, the hazard ratio of a positive MTWA was 19.7 on multivariate analysis (10). Only a few patients (9%) tested MTWA indeterminate, and those patients did not have an arrhythmic event. Although MTWA yielded a high sensitivity (83%), the positive predictive value of the test was only 9% and thus lower than in studies involving cardiomyopathy patients, whereas its negative predictive value (99.6%) was comparable to that in patients with reduced LVEF.

The present study has some limitations that make extrapolation of the results to other MI populations treated according to contemporary therapy guidelines difficult. First, there was an unusually frequent use of class I antiarrhythmic drugs (7%) in the present population, mainly for therapy of atrial arrhythmias. These drugs are generally not given early after MI in Western patient populations because of potential pro-arrhythmic hazards. Being aware of this, the authors performed separate analyses of statistical descriptors of MTWA for patients with and without specific antiarrhythmic therapy, showing that in this population of consequently revascularized patients, class I drugs had no negative effect on survival or on the predictive accuracy of MTWA testing. Second, there is a low prevalence of beta-blocker treatment in this population (21%). Because beta-blockers are a mainstay of post-MI therapy in the U.S. and Europe, with a highly beneficial impact on prognosis, both the incidence of serious arrhythmic events and the predictive power of MTWA may be different in other MI...
populations. Thus, the results of this prospective study warrant confirmation in a large trial in patients treated according to contemporary therapy guidelines.

In summary, the study by Ikeda et al. (10) provides new insights into the clinical problem of arrhythmia risk stratification in the setting of preserved LVEF. In this context, the present study is well in line with other publications which address post-MI mortality prediction in patients with better preserved LVEF (11). With the relatively low positive predictive value of MTWA alone, however, further studies are necessary to better define its role, possibly in combination with 1 additional electrocardiogram-based parameter, in selecting post-MI patients with preserved LV function who may benefit from primary prevention antiarrrhythmic interventions. According to the epidemiology of sudden cardiac death, the goal of arrhythmia risk stratification in the future will be 2-fold: 1) to identify those patients from high-risk populations who may not benefit from primary preventive ICD therapy and 2) to improve identification of patients from lower-risk populations who may suffer serious arrhythmic events and in whom ICD therapy will be beneficial. Whether this will translate into a better capability of preventing sudden death in such patient populations (12) remains to be determined in future interventional trials.

Reprint requests and correspondence: Dr. Thomas Klingenheben, Praxis für Kardiologie, Alfred-Bucherer-Str. 6, D-53115 Bonn, Germany. E-mail: Klingenheben@aol.com.

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