Editorial

Inducible Fast Ventricular Tachycardia After ST-Segment–Elevation Myocardial Infarction

Is Ventricular Tachycardia Ever Ok?

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Although our understanding of sudden cardiac death (SCD) is far from complete, at least part of SCD post–myocardial infarction (MI) is because of ventricular tachycardia (VT) that degenerates to ventricular fibrillation. Because of the poor outcome of resuscitative efforts, considerable effort has been directed at risk stratification to guide interventions to prevent and to protect patients from this syndrome. Several clinical and laboratory variables (structural, arrhythmic, and autonomic) have been associated with poor outcome; how to use these to determine which patients are likely to have SCD, for which we have an established primary prevention treatment strategy, versus non-SCD remains elusive.

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Ventricular ectopy was first recognized as a predictor of death in 1969; ventricular ectopy recorded on a standard ECG in outpatients were associated with a 6-fold increase in sudden death.[1] For patients with early post-MI, Lown et al[2] postulated that an electric catastrophe is more likely when ventricular premature beats occur early in the cycle, in salvos of ≥2, when they are multiform, or with a frequency >5/min. Ruberman et al[3] showed that complex premature beats were associated with a risk of sudden coronary death 3× that for men free of these findings. A graded prognostic importance of ventricular premature beats and left ventricular dysfunction was described in the Myocardial Post-Infarction Program.[4] The risk of nonsustained VT lasting 4 to 7 beats in the setting of acute coronary syndromes persists today as shown in the Metabolic Efficiency with Ranolazine for Less Ischemia in Non-ST-elevation Acute Coronary Syndrome-Thrombolysis in Myocardial Infarction 36 (MERLIN-TIMI 36) study.[5]

Programmed electric stimulation (PES) arose as a way of mimicking spontaneous ectopy and subjecting it to formal study. The pioneering work of Wellens, Josephson and others suggested that inducibility indicated reentry as a mechanism of VT and that suppressing induction with antiarrhythmic agents might prevent spontaneous VT and improve prognosis.[6,7] These observations were formative for our discipline, have been supported by many investigators, including in the present era, and are understood as truth to this day: spontaneous or inducible VT in patients with healed infarction confers significant risk. However, attempts to use spontaneous or inducible VT to inform management strategies have almost routinely failed, first with antiarrhythmic drugs and more recently with implantable cardioverter-defibrillator (ICD) therapy. The Cardiac Arrhythmia Suppression Trial (CAST) taught us that ventricular ectopy suppression does not improve survival.[8] Although intended as a comparison of Holter-guided and PES-guided therapy, the Electrophysiologic Study versus Electrocardiographic Monitoring (ESVEM) study demonstrated inability of each to predict freedom from recurrent ventricular arrhythmias with drug treatment.[9] This led to heated discussions about the specific details of what should constitute an adequate study but in retrospect should probably be interpreted as inherent and unavoidable limitations of the strategy itself.

In the first randomized controlled trial of PES to guide management for patients post-MI at risk for SCD, the Multicenter Unsustained Tachycardia Trial (MUSTT), patients without inducible sustained ventricular tachyarrhythmias had a significantly lower risk of sudden death or cardiac arrest and mortality than similar patients with inducible arrhythmias who were not treated with antiarrhythmic therapy.[10] However, because patients with inducible VT treated with ICDs fared better irrespective of whether or not an antiarrhytmic drug suppressed VT inducibility,[11] PES for risk stratification lost favor. The pendulum then swung to risk stratifying patients post-MI by the left ventricular ejection fraction (LVEF), as championed by the Multicenter Automatic Defibrillator Implantation Trial (MADIT) investigators.[12] The Defibrillators in Acute Myocardial Infarction Trial (DINAMIT) and Immediate Risk Stratification Improves Survival (IRIS) trial introduced the added difficulty that the dynamics soon after MI may change the efficacy of our most effective therapy for primary prevention.[13,14]

Many questions then and now remain unanswered: What is the relevance of early PES? How early is too early? Is the substrate stable? How long does the infarct take to heal? MUSTT used ≥4 days,[10] and the Medicare National Coverage Determination requires 1 month to have passed post-MI to use inducibility to justify payment for implantation of an ICD.[15] Duff et al[16] showed that in a dog model, time-dependent changes occur associated with a progressive decrease in inducibility of VT post-MI, and a critical determinant is the size of the MI itself. Bhandari et al[17] showed variability in the day-to-day reproducibility of inducibility post-MI. What defines inducibility? Our convention is to use 30 seconds of a ventricular tachyarrhythmia or intervention for hemodynamic compromise, but Mitchell et al[18] showed that the induction

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of <5 repetitive ventricular responses resulted in a lower probability of recurrence than the use of a criterion of <16 responses. And, what defines fast VT, the focus of the present investigation? When does VT become ventricular flutter? Viskin et al[19] considered monomorphic VTs with a cycle length ≤230 ms as ventricular flutter. Is any VT ok? One of us has argued that patients with hemodynamically tolerated, slow VTs should be treated with an ICD to reduce the risk of arrhythmic death.[20] This recommendation was based on the logic that any VT announces the potential for a cascade to SCD in a causality that we do not understand.

In this context, Zaman et al[21] report the significance of very fast VT (cycle length, 200–230 ms) induced at PES in patients with early reperfusion post-MI. Consecutive patients with ST-segment–elevation MI (median, 4 days post) referred for primary percutaneous coronary intervention and with a LVEF ≤40% underwent PES. An ICD was implanted for patients with inducible VT but not when the study was negative. The end point was the cumulative incidence of death or first arrhythmic event defined as resuscitated cardiac arrest or a spontaneous ventricular tachyarrhythmia. Of 1910 patients undergoing primary percutaneous coronary intervention, 1721 underwent LVEF assessment, and 414 had a LVEF ≤40%. PES was performed in 290 eligible patients: no arrhythmia or ventricular fibrillation/ventricular flutter with a cycle length <200 ms was induced in 203 patients (group 1) and monomorphic VT in 87 patients consisting of fast VT in 58 (67%, group 2) and slower VT in 29 (33%, cycle length >230 ms, group 3). At 4 years, by Kaplan–Meier analysis, the incidence of death or arrhythmia was 8.2±2.3%, 33.1±7.1%, and 37.0±10.2% in groups 1, 2, and 3, respectively. The authors concluded that in patients with early post–ST-segment–elevation MI the majority of inducible VT are fast VT, and this type of VT incurs at least a similar risk of arrhythmia or death as inducible slower VTs (cycle length >230 ms) and a significantly higher risk than patients with a negative PES.

Zaman et al[21] base their study on their rich, historical experience in this area for 2 decades. Notably, their stimulation protocol uses ≤4 extrastimuli, not commonly used by others, but they do emphasize that the significance of VT induced with this protocol is the same as VTs induced with ≤3 extrastimuli.[21] This article has many strengths. It is a contemporary look at PES post-MI. The protocol was rigorous and events carefully adjudicated. Most importantly, as pointed out by the authors, PES testing may provide a means to cull out truly high-risk patients early post-MI who might benefit from an ICD not identified in DINAMIT and IRIS. However, are we ready to readopt PES for risk stratification? We think that several limitations prevent acceptance of this view. First, as the authors admit, this study is observational in nature. Although it makes the point that inducible fast VT early after MI may be a marker of risk, data about the results of the strategy used (ICD implantation) cannot be properly interpreted in the absence of randomized data. In this regard, the authors' assertion that PES is a better risk stratifier than those used in DINAMIT or IRIS cannot be accepted. Second, the end points used in this investigation are potentially misleading. The majority of end points were episodes of appropriate ICD therapy, a metric that has been largely abandoned as it does not accurately indicate aborted SCD.[22,23] If events other than ICD therapies are excluded, the risk of total mortality is lower in group 1 than in the inducible groups (6.9%, 8.6%, 17.2% in the 3 groups, respectively; *P*=NS), but the majority of deaths were noncardiac. Finally, as a strategy, this approach had limited effect. The population included 1910 patients with ST-segment–elevation MI referred for percutaneous coronary intervention but ended with 79 patients receiving an ICD, 18 of whom received appropriate therapy.

Perhaps trite, this article leaves more questions unanswered than it answers: Is ventricular flutter really benign? One patient with ventricular flutter presented later with VT. Are PES-negative patients really safe? Three of 203 (1.5%) had arrhythmic events with 1 death and 1 with VT that stopped spontaneously. And for the PES-positive patients, 18 of the 20 events were ICD interventions, there was 1 sudden death, and 1 patient was resuscitated from a cardiac arrest and presumably that patient lived. Because ICD interventions overwhelmed SCD, would MADIT-RIT programming have changed the surrogate end point that included both device intervention and death?[24] Did ICD therapy cause harm in groups 2 and 3?

Our challenge now is that we still have the imperative to find better ways to risk stratify patients post-MI, as well as to craft successful treatment strategies, using this information. Although Buxton et al[25] and Goldenberg et al[26] have made first attempts using the MUSTT and MADIT-II databases, respectively, we have no prospective studies, and in the current environment, it will be hard to do such a study, but there is no reason why it cannot be done if carefully designed.[27] Furthermore, the incorporation of nonelectrophysiology metrics, such as peripheral arterial disease, might improve sensitivity and specificity of predicting prognosis.[28]

To conclude, although spontaneous and induced ventricular arrhythmias have long been recognized to be risk factors for both SCD, and indeed total mortality, interventions directed at arrhythmia markers themselves have been uniformly ineffective and often harmful. In this article, the majority of events were ICD detections and not death, and if these were taken away, total mortality dwarfs SCD. Although the authors make the point that their study is different from IRIS and DINAMIT, we interpret their findings as yet another demonstration that our risk stratifiers are not very good. Perhaps, if PES was married to a more sophisticated risk stratification algorithm using other markers, we could do a better job. So, is any VT Ok, spontaneous, or induced? For now, we will continue to use the LVEF as the primary metric to judge risk as it has been the basis for entry into all the primary prevention randomized controlled trials for ICD therapy post-MI. However, there remains a desperate need for a prospective, randomized controlled trial for risk stratification, incorporating clinical variables obtained at the bedside, measurements of autonomic tone, and electrophysiological study.

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