EDITORIAL COMMENT

Why Are (Only) Some Infarcted Hearts Arrhythmogenic?*

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In this issue of the Journal, Haqqani et al. (1) provide valuable insight as to why some patients who survive a large myocardial infarction (MI) are prone to ventricular tachycardia (VT), yet other survivors of a similar infarct are seemingly immune. They compare 17 patients presenting with recurrent, sustained monomorphic ventricular tachycardia (SMVT) with 17 post-MI patients undergoing prophylactic implantable cardioverter-defibrillator (ICD) insertion, who had so far been free from clinical episodes of SMVT. Notably, the SMVT and prophylactic ICD groups appeared nearly identical with regard to clinical characteristics (Table 1 in Haqqani et al. [1]), both being almost exclusively male, with equally depressed ejection fractions (0.28 and 0.26, respectively) and equally dilated ventricles. The SMVT group was, on average, 8 years older, and in view of recurrent SMVT, 16 were taking amiodarone, often in combination with a second antiarrhythmic agent. A slightly longer interval since (first known) MI (9 years vs. 8 years), a slightly longer QRS duration (144 ms vs. 132 ms), and a slight preponderance of inferior infarcts marked the VT group, but these differences did not approach significance in this relatively small study.

Why, then, had the SMVT patients “declared” themselves and the prophylactic ICD group not done so? The occurrence of an arrhythmia is often related to the confluence of a fixed substrate plus a functional, intermittent factor or trigger. Clearly, one would conclude from the information at hand (i.e., the apparently similar substrate of the 2 groups) that the reason for one group presenting with SMVT and the other not exhibiting VT would be explained by the occurrence or absence of triggers or such factors. One might (wrongly) conclude that the treatment should be directed at triggers, such as premature ventricular contractions, but that runs counter to the hard-earned lessons of CAST (Cardiac Arrhythmia Suppression Trial) (2). The trigger hypothesis also does not fit other data—the SMVT group was easily inducible into multiple VT morphologies, but the no-VT group was largely noninducible, even when triggers (programmed stimulation) were amply supplied (1). Despite the 2 groups’ apparently identical post-infarction clinical substrate, electroanatomic left ventricular mapping disclosed that the VT group had much more low voltage, and especially very low voltage (<0.5 mV), scar (1). Furthermore, more of the SMVT patients’ electrograms were fractionated or exhibited either isolated or very late potentials. Several groups (3–5) have reported similar findings based on epicardial and/or endocardial mapping at the time of aneurysm or VT surgery, but in these reports the non-VT group may not always have had as severe a cardiomyopathy (5).

The presence of prolonged, fractionated, and/or late, isolated electrograms in regions harboring VT circuits is thus not new. The infarct border zone harboring fractionated electrograms is known to be where VT can be targeted and eliminated, rather than the aneurysm itself. In the VT surgery era, resected, subendocardial infarct-border tissue typically contained 1 or more thin bundles of viable myocardium widely separated from one another by extensive fibrous tissue (6). Using tissue perfusion baths, mapping of such explanted specimens containing the map-determined SMVT site of origin has shown remarkably complex, “zig-zag” conduction (7). Despite extremely fractionated extracellular electrograms, intracellular recordings were typically normal and conduction velocity was brisk (0.7 m/s) along fiber orientation. However, transverse conduction meandered through the scar tissue along tenuous thin tracks one-tenth as fast. Actual conduction paths proved to be up to 18 times longer than the linear distance between 2 points (7).

The work of Haqqani et al. (1) reinforces earlier findings correlating propensity to VT with scarred regions harboring surviving isolated myocardial bundles from the pathologist’s perspective and fractionated, isolated electrograms as seen by the electrophysiologist (3–5). Others have shown that removing this tissue surgically or ablating it with a catheter targeting the abnormal potentials can be curative. This work emphasizes the primacy of substrate in determining whether VT will occur, and the fact that suitable VT substrate may or may not be present in similar sized infarcts. The older age of the SMVT group compared with the non-VT group and the possible tendency for increased time since infarct (not significant in this small study) could fit with what we know about fibrosis being progressive in the post-MI period (8) and for there to be a greater tendency for ICD benefit later after an infarct (9). Yet, we do not fully know why fibrosis continues to accumulate, how to predict those most at risk, or how to prevent it.

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Not surprisingly, a number of questions remain. Why do the non-VT patients in the study by Haqqani et al. (1) have fewer low voltage, abnormal electrogram sites, even though their ejection fractions are as depressed and theirventricles are as dilated? Do they have more intramural or subepicardial scar not as readily detected by endocardial mapping? But wouldn’t subepicardial scar be as prone to SMVT, as shown by many animal infarct models and even by human mapping (3)? It is interesting to speculate what magnetic resonance scans might have shown in the 2 groups. Recently, the likelihood of an ICD firing was found to correlate best with the amount of inhomogeneous scar (surrounding dense homogeneous scar), likely reflecting surviving fibers interspersed within scar tissue bordering an infarct (10). Patchy infarct has also been correlated pathologically with late post-infarct VT (11), perhaps because scattered, relatively larger sections of fibrosis cause more activation delay than an even greater amount of very fine, diffusely distributed, interstitial fibrosis (12). Last, does infarct location matter? This is a point raised by the slight excess of inferior infarcts in the SMVT group (nonsignificant) and the known arrhythmogenicity of mitral annular isthmus (13,14). Data such as that presented by Haqqani et al. (1) are scarce because patients without VT would undergo left ventricular mapping only for research purposes. Nevertheless, limitations must be kept in mind. Although well conducted, the study is small and essentially devoid of data specific to women surviving an MI, despite a climbing relative sudden death rate for women versus that in men (15). One cannot exclude the fact that amiodarone might have influenced the SMVT group’s electrograms. The relative propensity toward ventricular fibrillation may not be the same as that for SMVT by these criteria, since ventricular fibrillation risk may not correlate with inducibility of SMVT (16). Although the electroanatomic mapping methodology is widely used, the finding of low voltage is really only a histologic surrogate for scar, and may depend upon an amiodarone effect or the mapping modality used (17). In conclusion, the data of Haqqani et al. (1) stress the importance of the peri-infarct substrate in arrhythmogenesis. Future goals are to replicate and correlate this type of data with novel imaging and/or pathologic findings, and with arrhythmia events in follow-up in a similar but larger population, including women, as well as in nonischemic cardiomyopathy.

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REFERENCES


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