Idiopathic ventricular fibrillation (VF) is a disease of unknown etiology but with well described clinical (1) and electrophysiologic (2,3) characteristics. Briefly, young adults present with syncope or cardiac arrest due to polymorphic ventricular tachyarrhythmias in the absence of structural heart disease or identifiable channelopathies (4). The spontaneous arrhythmias are not related to stress and are invariably triggered by narrow-complex ventricular extrasystoles with very short coupling intervals (5,6).

Haïssaguerre et al. (7) recently reported that 1 of 3 patients with idiopathic VF has an intriguing electrocardiogram (ECG) that demonstrates J waves and ST-segment elevation in the inferolateral leads (the “early repolarization” pattern). In this issue of the Journal, Haïssaguerre et al. (8) report that “idiopathic VF patients with J waves” tend to develop arrhythmic storms that respond solely to isoproterenol and quinidine.

Le Syndrome d’Haïssaguerre

Patients with “idiopathic VF and early repolarization” were more often male subjects, had shorter QT intervals, and had arrhythmias more frequently than idiopathic VF patients with a normal ECG (7). High-amplitude J waves conferred a higher risk for arrhythmic storm, and transient augmentation of the J-wave amplitude preceded the onset of VF (7,8). These observations were confirmed by Nam et al. (9).

VF storms occur in 18% of patients with symptomatic Brugada syndrome (10) and occurred in 13% of idiopathic VF patients in this series (8). The VF storms of Brugada syndrome and idiopathic VF share some characteristics: VF clusters are sometimes triggered by fever, numerous VF episodes originate from the same myocardial area, and the recurrent arrhythmias are refractory to conventional antiarrhythmic therapy, including beta-blockers and intravenous amiodarone (8,10). Both conditions respond to intravenous isoproterenol (7–9,11), probably because isoproterenol reduces the dispersion of repolarization that enables the onset of VF (12). For all we know, patients with “idiopathic VF and early repolarization” have a worse (rather than a different) form of idiopathic VF.

The disappointing response to verapamil reported by Haïssaguerre et al. (8) is noteworthy because verapamil was the emergency treatment originally proposed for “short-coupled variant of torsade de pointes” (an arrhythmia indistinguishable from idiopathic VF) (13). In an instructive case (14), verapamil abolished the short-coupled extrasystoles that triggered VF (without prolonging the very short ventricular refractory period), while nifekalant prolonged the refractory period without suppressing the triggers of arrhythmia (14). Nonetheless, failure of verapamil has also been the rule in our experience (3).

The Fall and Rise of Quinidine

The excellent short- and long-term response to quinidine reported by Haïssaguerre et al. (8) should come as no surprise. Back in 1929, the first published case of idiopathic VF also involved an arrhythmic storm that responded to quinidine (15). For more than 2 decades (2), Belhassen (2,3,16–18) has led the way of quinidine therapy for idiopathic VF and Brugada syndrome with excellent results. Quinidine is also consistently effective during arrhythmic storms due to Brugada syndrome (11). In congenital short QT syndrome (a condition similar to idiopathic VF in many ways) (19), only quinidine (but not sotalol, flecainide, or ibutilide) normalizes the abnormally short ventricular refractory period and prevents the induction of VF (20). A prominent transient outward potassium current (I_{To}) plays a major role in arrhythmogenesis in these “J-wave syndromes” (21), and the beneficial effects of quinidine are probably mediated by I_{To} blockade (21).

Ironically, the realization that quinidine is often the only effective drug for VF storms comes at a time when it is increasingly difficult to obtain quinidine supplies (22). AstraZeneca, one of its main manufacturers, recently ceased production (23). As superbly summarized by Wilde and Langendijk (24), the disappearance of antiarrhythmic drugs like procainamide, mexiletine, and quinidine was driven by revenue issues and though affecting only a small number of patients, it may have dire consequences for them. Hopefully, this report by Haïs-
saguerre et al. (8) will prompt health care systems to negotiate with the pharmaceutical industry to ensure the availability of quinidine.

Who Is Afraid of the Big Bad J-Wave?

J waves are commonly observed in healthy individuals, predominantly in young males (25) and especially among athletes (26). These age- and sex-related differences persist during autonomic blockade with atropine and propranolol (25), suggesting that intrinsic differences in the contour of the myocardial action potential, secondary to sex-related diversity in ion-current density mediated by androgenic receptors (27), affect the size of J waves. The association between J waves and idiopathic VF described by Haïssaguerre et al. (7) was confirmed by Nam et al. (9) and our group (26) and is probably here to stay. In fact, the Haïssaguerre et al. study (7) triggered a “fear of J waves.” Electrophysiologists may be consulted about the arrhythmia-death risk after an incidental discovery of J waves. Unfortunately, we do not know how to distinguish “arrhythmogenic” from “normal” J waves. Haïssaguerre et al. (7) observed that patients with VF have J waves with larger amplitude than matched control subjects, and we noticed a similar trend (26). Also, patients with idiopathic VF have QT intervals in the lower normal range (19) that fail to prolong adequately during heart rate slowing (28). However, there is too much overlapping between VF patients and control subjects in terms of J-wave amplitude (7,26), J-wave location (26), and QT intervals to permit an accurate diagnosis. Finally, arrhythmias in idiopathic VF are not provokable by exercise but may be induced with programmed ventricular stimulation (1). Thus, electrophysiologists may be tempted to recommend electrophysiologic studies for risk stratification of patients with J waves (like current practices in Brugada syndrome) (29). That would be unadvisable because the value of VF induction for predicting spontaneous arrhythmias remains contentious (30). Since idiopathic VF is a rare disease, and there are no tests for confirming or excluding it in the asymptomatic patient, asymptomatic patients with J waves should not undergo further testing. During the last decade, numerous young and otherwise healthy individuals worldwide underwent prophylactic implantation of defibrillators because of “asymptomatic Brugada syndrome with inducible VF” (31). Yet, the consequences of that policy—in terms of adverse events—are only now being appreciated (30). Hopefully, patients with “asymptomatic J waves and inducible VF” will not share the same fate.

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