

if VT/VF is the cause of symptoms and to guide further therapy. Induction of VT/VF is often attempted before catheter ablation of the arrhythmia substrate to guide the procedure and to determine the success of the intervention after ablation is performed. An electrophysiological study can be used to determine the mechanism of a wide complex tachycardia. See Sections 7.3, 7.4, 7.6, 7.9.1.3, and 10.8 for recommendations regarding electrophysiological study for specific disease states.

## Recommendation-Specific Supportive Text

1. A study of electrophysiological testing in patients with symptomatic NICM found inducible VT/VF in 28% of patients which was associated with a higher rate of ICD events during follow-up.<sup>S4.3.2-17</sup> In a prospective cohort of 180 patients with ischemic or NICM and syncope, induction of VT or VF at electrophysiological study correlated with cardiac mortality only in patients with ischemic heart disease. In patients with NICM, cardiac mortality correlated with LVEF but not with inducibility on electrophysiological study.<sup>S4.3.2-18</sup>
2. In patients who meet criteria for ICD implantation (ie, HF and LVEF  $\leq 35\%$ ), data do not support the routine use of electrophysiological study solely for risk stratification, as such patients have been shown to derive survival benefit from the ICD.<sup>S4.3.2-8–S4.3.2-11</sup> An electrophysiological study may be helpful, however, in selected patients suspected to have preexcitation or supraventricular arrhythmias as the cause of symptoms or wide complex tachycardias that warrant definitive diagnosis and management. SVT leading to VT/VF or aberrantly conducted SVT may also be suspected in younger patients or those with a preserved LVEF. Induction of SVT and ablation may then be curative, with no need for an ICD. In such cases, failure to induce VT/VF after elimination of the substrate for SVT would be expected.
3. Risk stratification for channelopathies is generally made on the basis of symptoms, the ECG,<sup>S4.3.2-13, S4.3.2-19–S4.3.2-24</sup> exercise treadmill testing,<sup>S4.3.2-25–S4.3.2-27</sup> and the results of genetic testing.<sup>S4.3.2-28–S4.3.2-32</sup> The electrophysiological study (ie, programmed ventricular stimulation) does not have prognostic value for risk stratification in patients with these cardiac channelopathies.<sup>S4.3.2-12–S4.3.2-15</sup>

## 5. THERAPIES FOR TREATMENT OR PREVENTION OF VA

### 5.1. Medication Therapy

With the exception of beta blockers (eg, metoprolol succinate, carvedilol), there is no evidence from RCTs

that antiarrhythmic medications for VA improve survival when given for the primary or secondary prevention of SCD. However, the use of these medications is essential in some patients to control arrhythmias and improve symptoms. Medication use for VA is discussed, and any recommendations are listed, in subsequent sections. Further, medication-induced proarrhythmia is addressed in Section 10.7.

Antiarrhythmic medications are often categorized by the Vaughan Williams 4-level schema (class I: fast sodium channel blockers; class II: beta blockers; class III: repolarization potassium current blockers; class IV: nondihydropyridines calcium channel blockers).<sup>S5.1.5.2-1</sup> This system does not address the complexities in antiarrhythmic medications, since nearly every agent has multiple effects. Table 7 shows uses, electrophysiological effects, pharmacological effects, and common adverse effects of antiarrhythmic medications.

#### 5.1.1. Medications With Prominent Sodium Channel Blockade

Except in specific circumstances, sodium channel blockers (Vaughan-Williams class I agents) have a limited role in the prevention of VT/SCD; this is based on a lack of survival benefit and increased mortality observed during chronic therapy in patients with ischemic heart disease (see Section 10.7). Specific circumstances where sodium channel blockers have been used to treat VT/SCA include: intravenous lidocaine for patients with refractory VT/cardiac arrest (especially witnessed)<sup>S5.1.5.2-3</sup>; oral mexiletine for congenital long QT syndrome<sup>S5.1.5.2-4</sup>; quinidine for patients with Brugada syndrome; and flecainide for patients with catecholaminergic polymorphic ventricular tachycardia.<sup>S5.1.5.2-5</sup> These medications could also be used in ICD patients with drug- and ablation-refractory VT.

One newer medication of potential benefit, based on very limited data, is ranolazine. This medication, developed and FDA-approved as an antianginal agent, provides relatively specific late sodium channel current blockade in addition to less potent blockade of the phase 3 repolarizing potassium current; that is, the rapid delayed rectifier potassium current; IKr. The potential for clinical antiarrhythmic efficacy is supported by basic studies and experimental models.<sup>S5.1.5.2-6</sup> Clinical data are scant. In a study of 12 patients, ranolazine reduced ICD shocks in otherwise medication-resistant VT/VF in 11 patients.<sup>S5.1.5.2-7</sup> In MERLIN TIMI-36 (Metabolic Efficiency With Ranolazine for Less Ischemia in Non-ST-Elevation Acute Coronary Syndromes-Thrombolysis In Myocardial Infarction 36), ranolazine did not reduce SCD but did reduce VT in the first few days after a non-ST-segment elevation ACS.<sup>S5.1.5.2-8</sup> In 1 RCT, high-risk ICD patients with ischemic or NICM were randomly assigned to ranolazine 1000 mg twice a day versus placebo.<sup>S5.1.5.2-9</sup> High risk was defined as: 1) having a primary prevention