Management of Gene-Positive Catecholaminergic Polymorphic Ventricular Tachycardia: Are the Long Term Outcomes on Therapy Really So Poor?

To the Editor:

We read with great interest the article by Kawata et al on the long-term outcomes of catecholaminergic polymorphic ventricular tachycardia (CPVT) patients on treatment.¹ The authors are to be congratulated for their detailed analysis, and for highlighting the ongoing challenges related to CPVT treatment. There were several important points that we thought warranted specific mention.

First, the Japanese cohort consisted almost entirely of proband cases (32/34 patients, 94%). This supports the concept that probands with inherited heart rhythm disorders have more severe phenotypes than their affected relatives. Our group reported that CPVT probands are at a significantly higher risk of syncope ($P<0.001$), cardiac arrest ($P<0.001$) and treatment failure ($P=0.008$) compared with non-proband cases.² Relatives of CPVT patients are at low risk of fatal arrhythmia during long-term follow-up.³ The Kawata et al study, like our study and most of the literature to date, is affected by this bias, which highlights the need for systematic cascade screening and reporting of first-degree relatives.

Second, in contrast to emerging literature, the outcomes of flecainide are less favorable in the Kawata et al study. While the authors reported liberal use of flecainide (60% of subjects), 14 of 15 patients (92.9%) had high-risk breakthrough ventricular arrhythmia (VA) after initiation, including 21.4% with a fatal event. This is in contrast to recent data on approximately 150 severely affected CPVT patients who had largely excellent outcomes, predominantly on flecainide- β blocker combination regimens.⁴

Why do these patients have a seemingly poor response to flecainide? One contributing factor may be the inclusion of both ventricular bigeminy and couplets in the high-risk VA definition. It is not known whether complete suppression of these milder forms of VA actually decreases the risk of death, and most studies do not classify bigeminy and couplets as treatment non-responsiveness. If both these VA are removed from the definition, the incidence of high-risk VA (defined as bidirectional VT or polymorphic VT/ventricular fibrillation) decreases from 92.9% (13/14) to just 21.4% (3/14) on flecainide. In addition, 2 of 14 patients were taking flecainide as monotherapy, and although isolated data suggest that this may

be somewhat protective,⁵ it is not currently recommended. If two patients are removed from the analysis (1 patient taking flecainide monotherapy and 1 who was non-adherent), only one of the remaining 12 patients on flecainide (8.3%) had a fatal event.

We agree with the concluding remarks by Kawata et al indicating that left cardiac sympathectomy would be an appropriate adjunctive therapy for several of their patients, especially in the light of recent data from Italy.⁶ As such, the long-term prognosis of CPVT patients adherent to optimal treatment, including sympathetic denervation when indicated, is likely more favorable than suggested by Kawata et al. Further work is needed to determine long-term treatment outcomes in a larger, more heterogeneous population of CPVT patients including non-proband and genetically elusive cases. We believe that these factors are important to consider when counselling patients and evaluating therapy for CPVT.

References

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