

## Response to Letter Regarding Article, “Outcome of Apparently Unexplained Cardiac Arrest: Results From Investigation and Follow-Up of the Prospective Cardiac Arrest Survivors With Preserved Ejection Fraction Registry”

We would like to thank Professors Jáimez and Sánchez for their letter of response commenting on our recent summary of evaluation and outcome of our first 200 unexplained cardiac arrest probands.<sup>1</sup> We would first like to point out that we excluded patients with a manifest diagnosis, so none of these patients had overt evidence of an ion channelopathy or cardiomyopathy that are typically both readily diagnosed and treated. This is reflected in our empirical strength of diagnosis framework, which is necessary when a classic diagnosis is not forthcoming.<sup>2</sup> In addition, registries do not mandate care but rather capture it, and reflect the reality of practice with the vagaries of contextual clinical decision making.

In response to the concerns about the incidence of shocks and the inefficacy of medical therapy, it is important to point out the difference between efficacy and effectiveness. Without a doubt, a patient who is adherent to  $\beta$ -blockers for long QT syndrome has an extremely low risk of receiving a shock from their implantable cardioverter defibrillator (efficacy). In contrast, many patients do not adhere to recommended medical therapy, particularly when the patient is young and the diagnosis is not compelling (not effective). In our study, 3 of 18 patients diagnosed with long QT and 1 of 10 patients diagnosed with catecholaminergic polymorphic ventricular tachycardia received an appropriate shock. Several patients were on metoprolol before the recent evidence of inefficacy of metoprolol. All 4 patients had adjustment or initiation of medical management and have not received further shocks during follow-up. The  $\beta$ -blocker use in the undiagnosed patients reflects inclusion of weak evidence of disease patients, who may have had a single-prolonged QT interval or QTc prolongation in response to epinephrine, but no other evidence from exercise or genetic testing. These patients are often placed on empirical  $\beta$ -blockade.

A valid point is raised with regard to implantable cardioverter defibrillator programming, which again reflects an era of early intervention programming that has evolved in our study as it has in all practices.<sup>3</sup> We did not capture these details and are embarking on data collection to compare the 2 programming eras once sufficient outcomes have been accumulated. Finally, we began a focus on enrolling more family members 3 years ago, and currently have an analysis under consideration that involves 200 unexplained cardiac arrest first-degree relatives. This is a clear priority to understand family implications and enrich gene discovery opportunities.

### Disclosures

None.

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