

Reply to “Pro-arrhythmia with Anti-arrhythmic Drugs in Patients with Idiopathic Ventricular Arrhythmia: A Common Problem with Vague Definitions and Complex Interactions”

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Title: Reply to “Pro-arrhythmia with Anti-arrhythmic Drugs in Patients with Idiopathic Ventricular Arrhythmia: A Common Problem with Vague Definitions and Complex Interactions”

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Drs. Hasdemir and Payzin have cogently brought up one of the primary challenges in studying patients with frequent premature ventricular complexes (PVCs) and evaluating the impact of therapy. They highlight, based on their prior study,(1) that a group of patients may actually experience a significant increase in PVC burden (>50%) with medical therapy, which obviously raises concerns that this may enhance deleterious effects of PVCs, particularly in the long term.

With the advent of ambulatory monitoring, it was recognized early that PVC burden could be highly variable, leading to measurement error when using a 24-hour monitor. This error is highest when performing before-and-after studies of the effect of intervention on PVC burden, using single monitoring periods of 24 hours prior to and after intervention. In particular, spontaneous reductions in PVC burden can overestimate treatment effects. This error can be minimized in two ways, through serial monitoring (repeated measures)

or longer-term monitoring (>48h). Indeed, an elegant study by Dr. Mullis and colleagues, using 14 day patch monitors, showed a median absolute day-to-day fluctuation in PVC burden of almost 10% among patients with a high burden of PVC.(2) Thus, an apparent “pro-arrhythmic” effect of a medication may simply reflect inefficacy and expected variation in PVC burden.

In our prior work,(3) published in this journal and referenced by Drs. Hasdemir and Payzin, we were also limited by using only 24-hour ambulatory monitors to assess PVC burden. However, we did include a control group on no medical therapy, to mitigate the effect of measurement error, by obtaining an estimate of variation in PVC burden in the absence of therapy. In our study, we observed a “pro-arrhythmic effect” (>50% increase in PVC burden), in 2.5% (1/40) of patients on no medical therapy, 7.5% (4/53) on beta blockers/calcium channel blockers and 11.1% (3/27) on class I/III antiarrhythmic therapy. Despite the trend, these were not significantly different ($p=0.28$ and $p=0.14$ for beta blocker/calcium channel blocker and class I/III antiarrhythmics versus no therapy).

This does not negate a potential pro-arrhythmic effect of medical therapy in a minority of patients. However, more definitive proof of a pro-arrhythmic effect, distinguishing this from spontaneous variation in PVC burden, would require demonstration of a decrease in PVC burden with cessation of therapy. This would best be accomplished with a blinded, cross-over trial design.

Drs. Hasdemir and Payzin remind us to always critically assess, and reassess, our therapies for patients with frequent PVCs. We must always evaluate whether treatment is warranted (in the majority of cases it is not), and whether patients are at risk for adverse events, particularly from class I and III antiarrhythmics. Frequent PVCs make physicians uncomfortable but we should not rush to treatment and expose patients to unnecessary harm.

References:

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