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## Long-Term Effectiveness of Beta Blocker and Calcium Blocker Combination Therapy in Patients with CPVT

<u>Rosso, R</u><sup>1</sup>; Kalman, J<sup>1</sup>; Rogowsky, O<sup>2</sup>; Diamant, S<sup>2</sup>; Birger, A<sup>2</sup>; Biner, S<sup>2</sup>; Belhassen, B<sup>2</sup>; Viskin, S<sup>2</sup>

<sup>1</sup>The Royal Melbourne Hospital, Melbourne, Australia; <sup>2</sup>Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Introduction: The mainstay of therapy for catecholaminergic polymorphic ventricular tachycardia (CPVT) is maximal doses of <sup>2-</sup>-blockers (BB). However, recent data suggests that the 10-year risk for cardiac arrest despite <sup>2-</sup>-blocker therapy approaches 10%. Since the ventricular arrhythmias in CPVT are caused by calcium overload, we speculated that the combination of verapamil plus BB (V+BB) would be more effective than BB alone for suppressing ventricular arrhythmias. Indeed, we recently reported that V+BB effectively suppresses exercise-induced ventricular arrhythmias in patients refractory to BB alone. In the present study we report the long-term clinical follow-up of our original series. Methods: Six patients with CPVT who had exercise induced ventricular arrhythmias despite maximally tolerated doses of BB received V+BB. The combination therapy resulted in significant reduction of exercise-induced ventricular arrhythmias: (1) 3 patients had nonsustained ventricular tachycardia (VT) on <sup>2-</sup>-blocker, and none of them had VT on V+BB. (2) The number of ventricular ectopics during the whole exercise test went down from 7859±, beats to  $68\pm$ , beats. The patients were follow-up every 6 months and in case of recurrent symptoms.

Results: During a mean follow up of  $376\pm$ , months, three patients experienced recurrent arrhythmic symptoms including recurrent syncope in one, cardiac arrest in the second and appropriate ICD therapy in the third.

Conclusion: Despite a more effective suppression of exercise induced ventricular arrhythmias with V+BB, this combination therapy failed to prevent clinically significant ventricular arrhythmias during long-term follow-up. Suppression of exercise induced ventricular arrhythmias is a poor surrogate of long-term effectiveness of medical therapy in CPVT.