Predictors of myocardial recovery in pediatric tachycardia-induced cardiomyopathy

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BACKGROUND Tachycardia-induced cardiomyopathy (TIC) carries significant risk of morbidity and mortality, although full recovery is possible. Little is known about the myocardial recovery pattern.

OBJECTIVE The purpose of this study was to determine the time course and predictors of myocardial recovery in pediatric TIC.

METHODS An international multicenter study of pediatric TIC was conducted. Children $\leq$18 years with incessant tachyarrhythmia, cardiac dysfunction (left ventricular ejection fraction [LVEF] $<$50%), and left ventricular (LV) dilation (left ventricular end-diastolic dimension [LVEDD] z-score $\geq$2) were included. Children with congenital heart disease or suspected primary cardiomyopathy were excluded. Primary end-points were time to LV systolic functional recovery (LVEF $\geq$55%) and normal LV size (LVEDD z-score $<$2).

RESULTS Eighty-one children from 17 centers met inclusion criteria: median age 4.0 years (range 0.0–17.5 years) and baseline LVEF 28% (interquartile range 19–39). The most common arrhythmias were ectopic atrial tachycardia (59%), permanent junctional reciprocating tachycardia (23%), and ventricular tachycardia (7%). Thirteen required extracorporeal membrane oxygenation (n = 11) or ventricular assist device (n = 2) support. Median time to recovery was 51 days for LVEF and 71 days for LVEDD. Two (4%) underwent heart transplantation, and 1 died (1%). Multivariate predictors of LV systolic functional recovery were age (hazard ratio [HR] 0.61, $P = .040$), standardized tachycardia rate (HR 1.16, $P = .015$), mechanical circulatory support (HR 2.61, $P = .044$), and LVEF (HR 1.33 per 10% increase, p=0.005). For normalization of LV size, only baseline LVEDD (HR 0.86, $P = .008$) was predictive.

CONCLUSION Pediatric TIC resolves in a predictable fashion. Factors associated with faster recovery include younger age, higher presenting heart rate, use of mechanical circulatory support, and higher LVEF, whereas only smaller baseline LV size predicts reverse remodeling. This knowledge may be useful for clinical evaluation and follow-up of affected children.

KEYWORDS Supraventricular tachycardia; Catheter ablation; Antiarrhythmic drugs; Cardiomyopathy; Ventricular remodeling

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ABBREVIATIONS CI = confidence interval; **EAT** = ectopic atrial tachycardia; **EF** = ejection fraction; **HR** = hazard ratio; **LVEDD** = left ventricular end-diastolic dimension; **LV** = left ventricle; **LVEF** = left ventricular ejection fraction; **PJRT** = permanent junctional reciprocating tachycardia

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Introduction

Tachycardia-induced cardiomyopathy (TIC) has been defined as myocardial dysfunction that is wholly or partially reversible after control of the responsible tachyarrhythmia.[1] Despite a favorable clinical course for most patients,[2] reports of sudden cardiac death,[3–6] rapid deterioration in ventricular function with recurrence of tachyarrhythmia,[6] and significant delays in reverse remodeling ("persistent negative remodeling")[7–12] despite successful arrhythmia therapy have been described.

Much of the understanding of TIC is derived from animal models, in which dilated cardiomyopathy develops after 1 to 2 months of chronic rapid pacing.[13] Although cardiomyopathic changes have been firmly established in these controlled experiments,[13,14] clinical TIC is believed to develop and regress more unpredictably depending on variable patient and clinical factors.[15,16] To date, no large systematic clinical studies of this process have been conducted, so an understanding of the time course and predictors of myocardial recovery is lacking.[16,17] This knowledge is expected to be meaningful in terms of prognosis, clinical follow-up, and the need for ongoing heart failure management.[11,12]

Based on these considerations, we sought to characterize the myocardial recovery pattern in pediatric TIC. A multicenter study was conducted with the primary aim of analyzing 2 main indices of recovery: (1) left ventricular (LV) systolic function and (2) reverse remodeling. Secondary aims were to determine the responsible tachycardia substrates, efficacy of therapeutic strategies, complications related to such therapies, and adverse outcomes in a pediatric TIC cohort.

Methods

Cardiology databases at participating centers were explored for pediatric TIC cases, defined as children <18 years of age with ejection fraction (EF) $<50\%$ (according to previously published criteria[15]) and left ventricular end-diastolic dimension [LVEDD] ≥ 2 SD above the mean associated with incessant tachyarrhythmia. Premature ventricular contraction–induced cardiomyopathy was not considered in this definition. The incessant nature of the rhythm was documented by ambulatory monitoring $\pm$ inpatient telemetry demonstrating $\geq 75\%$ tachycardia burden. Each patient underwent formal diagnosis of the arrhythmia by either standard electrocardiographic criteria[18–20] or invasive electrophysiologic study demonstrating a nonsinus tachycardia mechanism (subsequently reviewed and adjudicated by 2 experienced electrophysiologists at the coordinating center). That the cardiomyopathy was secondary to the tachyarrhythmia was supported by retrospective observation of marked echocardiographic improvement (resultant left ventricular ejection fraction [LVEF] $\geq 55\%$ or absolute improvement in LVEF $\geq 20\%$) after successful tachyarrhythmia treatment. Patients were excluded from the analysis if there was evidence of congenital heart disease, genetic or familial cardiomyopathy, or other identifiable factor contributing to the cardiomyopathy either at presentation or during follow-up.

De-identified data electronically transferred to the coordinating center included baseline demographics, symptom severity (graded 0–4 based on Ross/New York Heart Association classification[1]), referring diagnosis, use of heart failure medication, inotropic or mechanical circulatory support, a copy of the initial ECG of tachyarrhythmia, and results of the presenting echocardiogram (including LVEDD, left ventricular end-systolic dimension, EF, and degree of mitral regurgitation). Initial and subsequent treatment strategies, including all procedural reports, were evaluated, as well as the type of response and complications related to medical and interventional therapy. Response to therapy was graded as complete (restoration of sinus rhythm without detectable tachycardia recurrence), partial ($\geq 50\%$ reduction in tachycardia burden), or none ($<50\%$ reduction in tachycardia burden) during initial inpatient and subsequent routine ambulatory ECG monitoring. Rate control (ongoing atrial tachyarrhythmia with slowing of AV nodal conduction and the resulting ventricular rate) was considered as partial success. To evaluate the myocardial recovery pattern, each center was asked to provide follow-up echocardiographic data at each subsequent examination until all parameters had completely normalized or the patient was no longer followed at that center.

After obtaining approval from the local institutional review board, each center transmitted the data to the primary center at UCLA through a secure, web-based application (Research Electronic Data Capture, REDCap).

Statistical analysis

The primary outcome measures were time to (1) LVEF $\geq 55\%$ ("LV systolic functional recovery") and (2) normalization of LVEDD to within 2 SD of the mean ("reverse remodeling"). Time to normalization was calculated from the onset of antiarrhythmic drug effect or catheter ablation procedure to the primary end-point, the latter determined by linear estimation between successive echocardiographic studies of the respective outcome variable (LVEF or LVEDD). Both LVEDD and presenting heart rate were standardized (for body size and age, respectively) in order to accommodate normal changes in these values with growth. The standardized value is defined as the difference between the observed and the predicted values and is expressed as the standard deviation so that zero represents the population mean and $+2$ the upper limit of normal.