# Electrophysiologic characteristics and catheter ablation results of tachycardia-induced cardiomyopathy in children with structurally normal heart

Hasan Candaş Kafalı,
 Erkut Öztürk,
 Senem Özgür,
 Gülhan Tunca Şahin,
 Alper Güzeltaş,
 Yakup Ergül

Department of Pediatric Cardiology, University of Health Sciences, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital; İstanbul-*Turkey* 

# **ABSTRACT**

**Objective**: The aim of this study is to present electrophysiologic characteristics and catheter ablation results of tachycardia-induced cardiomy-opathy (TIC) in children with structurally normal heart.

Methods: We performed a single-center retrospective review of all pediatric patients with TIC, who underwent an electrophysiology study and ablation procedure in our clinic between November 2013 and January 2019.

Results: A total of 26 patients, 24 patients with single tachyarrhythmia substrates and two patients each with two tachyarrhythmia substrates, resulting with a total of 28 tachyarrhythmia substrates, underwent ablation for TIC. The median age was 60 months (2–214 months). Final diagnoses were supraventricular tachycardia (SVT) in 24 patients and ventricular tachycardia (VT) in two patients. The most common SVT mechanisms were focal atrial tachycardia (31%), atrioventricular reentrant tachycardia (27%), and permanent junctional reciprocating tachycardia (15%). Radiofrequency ablation (RFA) was performed in 15 tachyarrhythmia substrates, and cryoablation was performed in 13 tachyarrhythmia substrates, as the initial ablation method. Acute success in ablation was achieved in 24 out of 26 patients (92%). Tachycardia recurrence was observed in two patients (8%) on follow-up, who were treated successfully with repeated RFA later on. Overall success rates were 92% (24 out of 26) in patients and 93% (26 out of 28) in substrates. On echocardiography controls, the median left ventricular recovery time was 3 months (1–24 months), and median reversible remodeling time was 6 months (3–36 months).

Conclusion: TIC should be kept in mind during differential diagnosis of dilated cardiomyopathy. Pediatric TIC patients can be treated successfully and safely with RFA or cryoablation. With an early diagnosis of TIC and quick restoration of the normal sinus rythm, left ventricular recovery, and remodeling may be facilitated. (Anatol J Cardiol 2020; 24: 370-6)

Keywords: dilated cardiomyopathy, tachycardia-induced cardiomyopathy, pediatric, ablation therapy

#### Introduction

Dilated cardiomyopathy is most commonly seen in pediatric patients. Most of the cases are idiopathic. It is crucial to diagnose treatable anatomic and functional etiologies of idiopathic dilated cardiomyopathy (1, 2). Tachycardia-induced cardiomyopathy (TIC), characterized by incessant tachycardia, and congestive heart failure, is one of these etiologies (3).

TIC in pediatric patients is an important clinical diagnosis, determined by signs, and symptoms of ventricular dysfunction due to rapid or irregular rhythm, which can recover completely or partially if normal sinus rhythm is restored (4, 5). Tachycardia substrates with different supraventricular or ventricular

mechanisms like focal atrial tachycardia, permanent junctional reciprocating tachycardia, atrioventricular reentrant tachycardia, atypical atrioventricular nodal reentrant tachycardia, and ventricular tachycardia (VT) can cause TIC (3-5).

The goal of TIC is to restore the sinus rhythm aggressively to reverse cardiac functions and to reduce congestive heart failure symptoms. Accordingly, different antiarrhythmic combinations have been used, but, based on the recent reports in the literature, medical therapy has failed in most cases (6, 7).

Radiofrequency ablation (RFA) is a safe and effective method used in the definitive treatment of pediatric tachyarrhythmias. Recently, cryoablation has evolved as a safer and equally effective alternative to RFA (8). The success of ablation therapy in

Address for correspondence: Dr. Erkut Öztürk, İstanbul Sağlık Bilimleri Üniversitesi, Mehmet Akif Ersoy Göğüs Kalp ve Damar Cerrahisi Eğitim

ve Araştırma Hastanesi, Çocuk Kardiyoloji Kliniği, İstanbul-*Türkiye* Phone: +90 212 692 20 00 E-mail: erkut\_ozturk@yahoo.com

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pediatric tachyarrhythmia has been reported in the literature (8, 9). However, data about the results of ablation therapy in TIC are limited (3, 7).

This study aims to share our experience with ablative modalities (RFA and cryoablation) in children with TIC.

## **Methods**

In this retrospective study, patients with a diagnosis of TIC, resistant to medical therapy, and treated with ablation between November 2013 and January 2019 were reviewed. The study was approved by the Local Ethics Committee.

TIC patients less than 18 years of age with a left ventricular shortening fraction of less than 28% or ejection fraction of less than 55% in echocardiography and with a left ventricular end-diastolic diameter Z-score of more than or equal to two were included in the study. Primary dilated cardiomyopathy patients with sinus tachycardia and patients with an associated congenital heart defect were excluded.

Age at the time of diagnosis, sex, body weight, signs, and symptoms, tachyarrhythmia type, electrocardiography and echocardiography findings, 24-hour Holter electrocardiogram monitoring, antiarrhythmia medications, and details of ablation procedures were retrieved from Filemaker database system.

The echocardiographic assessment was performed as recommended by the American Society of Echocardiography guideline (10). A shortening fraction of less than 28% or an ejection fraction of less than 55% indicated systolic dysfunction. Patients who exhibited a left ventricular end-diastolic diameter Z-score of more than two with systolic dysfunction were classified as having dilated cardiomyopathy.

The standard 12-lead electrocardiogram was interpreted electronically with Muse system (Muse Cardiology Information System, GE Healthcare, USA). Tachycardia is defined as a heart rate (HR) that is in the 95<sup>th</sup> percentile or greater according to agespecific standard values. The 12-lead ECG, 24-hour Holter ECG recordings, and, if needed, electrophysiological study were used for the classification of arrhythmias. HR percentile was defined as HR/median HR for age, and PR index as the PR/RR interval. P-wave morphology was defined as possible sinus or nonsinus based on a predefined algorithm (6).

Each patient underwent a formal diagnosis of the arrhythmia either by standard electrocardiographic criteria or invasive electrophysiology study demonstrating a nonsinus tachycardia mechanism, similar to other studies (11-13).

Electrophysiology studies and catheter ablations were carried out under general anesthesia. Before the procedure, hemodynamically compromised patients were started on inotropic agents (milrinone as the first-line therapy, and noradrenaline as the second option). In all patients, invasive blood pressure monitoring was performed via radial or femoral arterial lines during the study. An electroanatomic mapping system (EnSite Velocity,

St. Jude Medical Inc., St. Paul, MN, USA) was used with limited fluoroscopy. Electrophysiologic catheters were inserted through the femoral and internal jugular vein, and sometimes, a transesophageal electrophysiological study catheter was used in infants. All patients received 75–100 IU/kg intravenous heparin during left-sided ablation procedures with RFA. We attempted catheter placement in the high right atrium, His bundle region, right ventricular apex, and coronary sinus for tachycardia mapping. Patent foramen ovale, if present, was used to gain access to the left atrium, or transseptal puncture with a curved Brockenbrough needle was performed if patent foramen ovale is not present. Standard atrial and ventricular stimulation protocols with single and double extra stimuli and burst pacing were used to induce tachyarrhythmia. If tachyarrhythmia could not be induced, orciprenaline was given with infusion. Incessant tachyarrhythmia was already present in most patients, and a complete atrial and ventricular protocol could not be performed before ablation. Standard diagnostic tests were performed to determine tachycardia mechanisms, tachycardia locations, and electrophysiological features of the tachycardia substrates. The following major complications were reported: bleeding or hematoma in vascular access site, temporary or permanent second- to thirddegree atrioventricular block, bundle branch block, pericardial effusion, profound bradycardia, or hypotension during the study, coronary artery injury, and cardiopulmonary resuscitation reauirement.

Success in ablation was defined as restoration of the normal sinus rhythm at the end of the procedure, and procedural failure was sustained tachycardia requiring ongoing medical therapy.

Follow-up after ablation was performed on the 1<sup>st</sup>, 3<sup>rd</sup>, 6<sup>th</sup>, 12<sup>th</sup>, 24<sup>th</sup>, and 36<sup>th</sup> months with standard 12-lead electrocardiograms, 24-hour ambulatory electrocardiogram if needed, and echocardiography for evaluation of cardiac function. Follow-ups were performed yearly thereafter with electrocardiogram and echocardiography.

Recurrence was defined as any tachycardia except sinus tachycardia, diagnosed on standard surface electrocardiogram or 24-hour ambulatory electrocardiogram, at any time after a successful ablation. "Left ventricle systolic functional recovery" was defined as left ventricular shortening fraction of greater than 28% or ejection fraction of greater than 55%, and "reverse remodeling" was defined as normalization of left ventricular end-diastolic diameter to within two standard deviations of the mean (6).

#### Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Science (SPSS, Chicago, Illinois, USA) Version 17.0 for Windows. The descriptive analysis (frequency, median, and range) was used to identify the general and specific features of the studied sample.

#### Results

## Study population characteristics

The inclusion criteria were met by a total of 26 patients. Of these 26 patients, 16 were male (61.5%). The median age was 60 months (ranging from 2 to 214), and the median weight was 21 kg (ranging from 2.5 to 85 kg). Seven patients were younger than 1 year, and 11 patients were between 1- and 5-year-old.

The most common presenting symptoms were congestive heart failure signs (42%) characterized by respiratory distress, diaphoresis, poor feeding, and palpitations (38%). Five patients had a wide QRS tachycardia. Median shortening fraction on echocardiography was 21% (ranging from 14% to 28%). In ten patients, shortening fraction was less than 20%. At least one intravenous inotrope was initiated in 38% of the patients. The demographic characteristics of the patients are summarized in Table 1.

#### **Arrhythmia classification**

Out of the 26 patients, 24 were classified as having supraventricular tachycardia (SVT), and two were classified as VT. The most commonly seen SVTs were focal atrial tachycardia (31%), atrioventricular reentrant tachycardia (27%), and permanent junctional reciprocating tachycardia (15%). SVT substrate locations were right atrium in 50% of the patients, left atrium in 42% of the patients, and atrioventricular node in 8% of the patients. Both of the ventricular tachycardias were originated from the left ventricle (Tables 1 and 2).

#### Medical therapy and catheter ablation

Before the ablation procedure, two and three antiarrhythmic combinations were used in 45% and 40% of the patients, respectively.

The initial ablation method was RFA in 13 patients and cryoablation in 11 patients. In two patients with additional tachyarrhythmia substrates, combined RFA, and cryoablation were used separately for each concomitant substrate. Irrigated RFA was performed successfully in a patient after the failure of the classic RFA. The cryoablation failed in another patient; subsequently, RFA was performed, which resulted in suboptimal success. In another patient, the failed RFA was followed by successful cryoablation (Table 2).

The median procedural time was 165 minutes (ranging from 72 to 310 minutes), and median fluoroscopy time was 5 minutes (ranging from 1.5 to 39.4 minutes). In seven patients, ablation with "zero fluoroscopy" was performed.

The ablation procedure was successful in 24 patients (92.3%) and suboptimally successful in two patients (ablation of multifocal atrial tachycardia in patients 20 and 25). Recurrence was observed in two out of 24 cases (8.3%) on follow-up. Successful RFA was performed in both of the recurrent patients.

In four patients, transseptal puncture was performed to ablate the left-sided tachycardia substrates.

Table 1. Baseline characteristics of the patients (n=26)	
Median age (months)	60 (2-214)
Median weight (kg)	21 (2.5-85)
Male gender	16 (63%)
Wide QRS tachycardia on admission	5 (19%)
Heart rate percentile on 24-hour ambulatory ECG (%)	155 (120-180)
Symptom on admission	
Heart failure symptoms*	11 (42%)
Palpitation	10 (38%)
Exercise intolerance	7 (27%)
Chest pain	6 (23%)
Syncope	3 (11%)
Echocardiographic findings	
SF (%)	21 (14-28)
EF (%)	35 (25-55)
Z-score for LVEDd	+3.1 (2.2-7)
Patent foramen ovale	4 (16%)
Initial management	
PCICU admission	7 (27%)
Inotropic support	10 (38%)
Mechanical circulatory support (ECMO)	-
Final tachyarrhythmia diagnoses (n=28)**	
FAT	8 (31%)
AVRT	7 (27%)
PJRT	4 (15%)
aAVNRT	3 (8%)
VT	2 (8%)
MAT	2 (8%)
Mahaim tachycardia	1 (4%)
AF	1 (4%)

Values are median (range) or n=(%). \*Respiratory distress, diaphoresis, and poor feeding. \*\*There were two patients with additional tachyarrhythmia substrate; one patient with MAT and AF and one patient with Mahaim tachycardia and aAVNRT. aAVNRT - atrioventricular nodal reentrant tachycardia; AF - atrial flutter; AVRT - atrioventricular reentrant tachycardia; ECMO - extracorporeal membrane oxygenator; EF - ejection fraction; FAT - focal atrial tachycardia; LVEDd - left ventricular end-diastolic diameter; MAT - multifocal atrial tachycardia; PCICU - pediatric cardiac intensive care unit; PJRT - permanent junctional reciprocating tachycardia; SF - shortening fraction; VT - ventricular tachycardia

There was no major complication requiring cardiopulmonary resuscitation or resulting in death. Overall, there were three complications: transient pericardial effusion during transseptal puncture in a 12-year-old patient with focal atrial tachycardia (patient 6), permanent incomplete right bundle branch block in a 3-month-old patient with a right anteroseptal/parahisian accessory pathways (patient 18), and one transient ST elevation during ablation in an 11-year-old patient with focal atrial tachycardia (patient 23). The procedural details are given in Table 2.

#### Follow-up

During the median follow-up time of 26 months (ranging from 7 to 64 months), the only SVT recurrence occurred in the patient with suboptimal response to ablation and under triple antiar-

rhythmic combination therapy with amiodarone, propafenone, and flecainide (patient 20). The other patient with suboptimal success (patient 25), who was under antiarrhythmic combination therapy with propranolol and flecainide, is still followed-up without any problem.

On follow-up of the patients with successful ablation, "left ventricle functional recovery" (shortening fraction greater than 28% or ejection fraction greater than 55%) and "reverse remodeling" (left ventricular end-diastolic diameter Z-score of less than +2) was observed by echocardiographic evaluation. In patients with suboptimal success, both "left ventricle functional recovery" and "reverse remodeling" were achieved in patient 20, whereas only "left ventricle functional recovery" was achieved in patient 25. The median duration for "left ventricle functional recovery" was 3 months (ranging from 1 to 24 months) and for "reverse remodeling" was 6 months (ranging from 3 to 36 months) (Table 2). In the seventh month of follow-up for the patient 25, shortening fraction was 28%, and left ventricular end-diastolic diameter Z-score was still +3 (Table 2).

# Discussion

In this study, we found that the most commonly seen tachyarrhythmias leading to TIC were focal atrial tachycardia, permanent junctional reciprocating tachycardia, and atrioventricular reentrant tachycardia associated with concealed accessory pathways. Ablation of these tachyarrhythmias was performed with high success and very low complication rates, and impaired left ventricular function was reversed in most of the patients. This is one of the few studies on the effect of ablation on pediatric TIC in the literature. Also, and to our best knowledge, this is the largest single-center pediatric cohort in ablation of TIC.

Despite intensive clinical research and advance, the management of cardiomyopathies is difficult in the pediatric age group. Dilated cardiomyopathy is the most common form and also the most common cause of heart transplantation in children (1, 2). Although most of the cases are idiopathic, a few etiological subgroups like an anomalous left coronary artery from the pulmonary artery and tachyarrhythmias are treatable and should be excluded (1, 14-16). Aykan et al. (7) reported 12 dilated cardiomyopathy patients secondary to TIC, while two of them were referred with a diagnosis of idiopathic dilated cardiomyopathy and one patient with a diagnosis of myocarditis.

In our study, three patients were referred with a diagnosis of idiopathic dilated cardiomyopathy, and one patient with myocarditis had experienced TIC. Two out of three had focal atrial tachycardia, and the other one had permanent junctional reciprocating tachycardia. The patient with "myocarditis" had multifocal atrial tachycardia. These findings support that dilated cardiomyopathy patients must be evaluated in detail for tachyarrhythmias as etiological factors.

The prevalence of TIC in pediatric population is not precisely known, because there are only a few cases in the literature. One diagnostic dilemma is which of the dilated cardiomyopathy and tachyarrhythmia being the primary disease leading to the other one (6, 7). There are a few studies in the literature to overcome this difficulty. Jeong et al. (15) compared 21 adult TIC patients with 15 idiopathic dilated cardiomyopathy patients (mean age 50±15 years). They claimed that a left ventricular end-diastolic diameter less than or equal to 61 mm could predict TIC with a sensitivity of 100% and a specificity of 71.4%. Gelb and Garson (4) compared 34 TIC patients with right atrial ectopic tachycardia and 33 idiopathic dilated cardiomyopathy patients with sinus tachycardia. They postulated that a resting HR greater than 150% of the predicted normal HRs is a key clinical parameter for differential diagnosis. Moore et al. (6) presented a retrospective study from 16 participating centers, comparing 80 pediatric TIC patients with 135 controls having idiopathic dilated cardiomyopathy. They had found that TIC cases demonstrated lower left ventricle end-diastolic and end-systolic diameter than controls, and were less likely to receive inotropic medication at presentation. HR percentile greater than 130%, PR index greater than 30%, and nonsinus P-wave morphology were associated with a sensitivity of 100% and specificity of 87% for the diagnosis of TIC. In our study, all the patients had a heart rate percentile greater than 120%, and in 24 of them greater than 130%.

The most common arrhythmias associated with pediatric TIC include focal atrial tachycardia, atrioventricular reentrant tachycardia, and permanent junctional reciprocating tachycardia. In contrast, atrial Şbrillation, atrial şutter, and persistent VT are more prevalent among adults and the elderly (17).

Moore et al. (3) reported a multicenter retrospective study from 17 participating centers, including 81 pediatric TIC patients. Focal atrial tachycardia (59%) and permanent junctional reciprocating tachycardia (23%) were the most common arrhythmias associated with TIC. There were only seven patients with ventricular arrhythmia in their study. Aykan et al. (7) reported permanent junctional reciprocating tachycardia (58.3%) and focal atrial tachycardia (41.6%) as etiological causes for TIC.

Focal atrial tachycardia (31%), atrioventricular reentrant tachycardia (27%), and permanent junctional reciprocating tachycardia (15%) were the most common arrhythmias leading to TIC in our study. Our results suggest that there might be a relationship between long RP tachycardias and TIC. In contrast to most adult studies, VT was rare, and no atrial fibrillation was diagnosed at all.

In the multicenter study reported by Moore et al. (3), ablation was performed in 55 out of 81 patients due to ineffective medical therapy. In 41 patients, only one ablation procedure was performed, and the procedure was repeated once in nine patients and twice in five patients because of recurrence,. Acute success was achieved in 48 patients (87%), suboptimal success in six patients (11%), and ablation therapy failed in one patient (2%).

Aykan et al. (7) reported a major complication rate of 2.6% and an overall complication rate of 7.2%. They reported an acute success rate of 66%, and the overall success rate increased to 91.6% with repeated RFA in the long term. In our study, the acute success rate of RFA or cryoablation was 92%. Suboptimal success was achieved in one patient with multifocal atrial tachycardia and concomitant atrial fibrillation and in one patient with multifocal atrial tachycardia only (8%). In two patients, repeated ablation was performed due to recurrence. There were no major complications and only three minor complications (11%). EnSite system was used in all patients, and in seven patients, no fluoroscopy was used.

TIC can be corrected partially or totally by rhythm and HR control; therefore, its early recognition is crucial. The recovery time of dilated cardiomyopathy following arrhythmia treatment varies based on the patient's age. Improvements can occur within a few weeks in infants, whereas it can take two to three years in older children. The duration of the remodeling depends basically on the duration of the tachycardia itself (3). Reversibility of cardiomyopathy after effective treatment is an important characteristic and has been studied in experimental models (18, 19). In pediatric TIC, the time to myocardial recovery after treatment has been incompletely described. Prior reports have described weeks to months for left ventricular systolic functional recovery, and even years for reverse remodeling (20, 21). De Giovanni et al. (16) evaluated the pattern of left ventricular recovery secondary to incessant tachycardia after RFA in a group of infants and children. Age at the time of ablation was 2 months to 12.5 years (mean 4.1 years). They concluded that the time of recovery was related principally with the duration of the tachycardia and was significantly shorter in infants. Moore at al. (3) reported "left ventricle functional recovery" in 92% and "reverse remodeling" in 88% of their patients. The median duration for left ventricular systolic function recovery and reverse remodeling was seven and ten weeks, respectively. They postulated that younger age, a higher HR, a higher left ventricular ejection fraction at admission, and the use of advanced life support systems were associated with shorter functional recovery time. In contrast, a shorter left ventricular diameter at admission was associated with a shorter remodeling time.

In our study, "left ventricle functional recovery" rate was 100%, and the remodeling rate was 96%. Duration of left ventricular functional recovery (median: three months) was shorter than that of left ventricular remodeling (median: six months). Younger age at admission was associated both with shorter functional recovery and remodeling time.

#### Study limitations

The main limitation of this study is a limited number of cases from a single-center. Other limitations are a relatively short follow-up period and standard follow-up times with controls apart from each other, causing a delay in the detection of the recovery and remodeling times.

# **Conclusion**

In conclusion, TIC must be kept in mind in the differential diagnosis of pediatric dilated cardiomyopathy as treatable cause. Transcatheter ablation (RFA or cryoablation) may contribute to shortening of left ventricular recovery and remodeling time.

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