Korean Circ J. 2024 Dec;54(12):865-867
https://doi.org/10.4070/kcj.2024.0417
pISSN 1738-5520·eISSN 1738-5555

kcj
Korean Circulation Journal

Editorial

Check for updates

Catecholaminergic Polymorphic Ventricular Tachycardia in Children: Insights and Challenges From the Current Study

Min-Jung Cho, MD

Department of Pediatrics, Gyeongsang National University Changwon Hospital, Changwon, Korea

▸ See the article "Treatment Outcomes in Children With Catecholaminergic Polymorphic Ventricular Tachycardia: A Single Institutional Experience" in volume 54 on page 853.

OPEN ACCESS

Received: Dec 6, 2024
Revised: Dec 17, 2024
Accepted: Dec 17, 2024
Published online: Dec 20, 2024

Correspondence to
Min-Jung Cho, MD
Department of Pediatrics, Gyeongsang National University Changwon Hospital, 11, Samjeongja-ro, Seongsan-gu, Changwon 51472, Korea.
Email: mjchomd@gmail.com

ORCID iDs
Min-Jung Cho
https://orcid.org/0000-0002-6884-853X

Funding
The author received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest
The author has no financial conflicts of interest.

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an uncommon inherited arrhythmia syndrome which can lead to sudden cardiac death especially in children and adolescents. It is characterized by bidirectional or polymorphic ventricular tachycardia (VT) during exercise or emotional stress, despite the absence of secondary issues such as structural cardiac abnormalities, electrolyte imbalances, or digoxin toxicity. It is estimated to occur in about 1 in 10,000 individuals, although the exact incidence is difficult to determine, as resting electrocardiograms may appear normal and imaging studies are often unremarkable. In this regard, the study recently published by Lee et al.[1] is noteworthy for its evaluation of the clinical and genetic characteristics of CPVT in the Asian cohort. Despite the rarity of the condition, the study provides valuable insights due to its long-term follow-up of a relatively significant number of patients.

In the study by Lee et al.,[1] they evaluated and emphasized the neurodevelopmental manifestations commonly associated with CPVT patients. These neurodevelopmental manifestations are known to be linked to mutations in the cardiac calcium release channel/ryanodine receptor gene (RYR2), which is a major causative mutation of CPVT. RYR2 is the cardiac isoform of the ryanodine receptor, but it is also widely expressed in the brain and plays a crucial role in intracellular Ca^{2+} signaling and homeostasis in the central nervous system.[2] As a result, CPVT patients with RYR2 mutations may exhibit a higher prevalence of learning and memory impairments compared to the general population.[3] It remains unclear whether neuropsychiatric manifestations are linked with an increased risk of malignant cardiac phenotypes in CPVT patients. However, it seems important to evaluate and manage not only arrhythmic issues but also neuropsychiatric symptoms and cognitive development when following up with CPVT patients.

Research is still ongoing to determine which characteristics in CPVT patients can predict a higher frequency of lethal tachyarrhythmias. As of now, there is no well-established scoring system like that for long QT syndrome. In the study by Lee et al.,[1] attempts were made to predict the risk of lethal arrhythmic events during follow-up of CPVT, from various perspectives. However, due to the retrospective nature of the study, treatment protocols for the patients varied significantly, which appears to limit the ability to draw clear conclusions.

Data Sharing Statement
The data generated in this study is available from the corresponding author upon reasonable request.

The contents of the editorial are the author's own views and do not necessarily reflect the view of the *Korean Circulation Journal*.

Current guidelines recommend that patients with CPVT should be primarily restricted from competitive exercise, and initiate treatment with beta-blockers, particularly non-selective beta-blockers such as nadolol or propranolol.[4] However, while β-blockers are the cornerstone of CPVT treatment, they are not fully effective in all patients. As highlighted in the study by Lee et al.,[1] flecainide is an effective medication that significantly reduces the burden of ventricular arrhythmias in CPVT patients. Therefore, if arrhythmias remain uncontrolled despite appropriate dosing of beta-blockers—manifesting as syncope, polymorphic or bidirectional VT, or exercise-induced ventricular ectopy—combination therapy with flecainide should be actively considered.[5]

In symptomatic patients who are not respond to adequate medical therapy, or who are unable to tolerate these medications, or if both drugs are contraindicated, sympathetic cardiac denervation (LCSD) should be considered.[4] For patients who experienced cardiac arrest, recurrent syncope, or polymorphic/bidirectional VT despite optimal medical therapy and/or LCSD, implantation of an implantable cardioverter-defibrillator (ICD) may also be considered.[4]

However, ICD shocks, whether appropriate or inappropriate, can provoke or exacerbate arrhythmias due to the catecholamine surge induced by the associated pain and fear. Furthermore, while ICD shocks effectively terminate ventricular fibrillation, they are generally unsuccessful in terminating polymorphic or bidirectional VT.[6] The question of whether LCSD or ICD should be prioritized, and whether LCSD could replace an ICD, remains a subject of ongoing debate with evidence supporting both approaches.[7][8] Lee et al.[1] observed a patient who underwent LCSD in combination with beta-blocker and flecainide therapy, but still experienced a near-fatal or fatal event. This observation supports the argument that LCSD may not fully prevent near-fatal or fatal events. However, as the authors themselves noted, the precision of the denervation surgery—particularly the extent and accuracy of the sympathetic nerve resection—could have influenced the final outcome. Therefore, it seems premature to draw a definitive conclusion based solely on this anecdotal finding.

Given the nature of CPVT, it is important to acknowledge the dual burden of ICD therapy; ineffectiveness and pro-arrhythmia. At the same time, the need for ICD therapy should be carefully considered for certain patients. Adherence to optimal medical therapy with β-blockers and flecainide, as well as meticulous ICD programming—such as setting high heart rate threshold for detection and maximizing the time window to identify episodes of polymorphic VT with a high likelihood of self-termination- are crucial to minimizing inappropriate shocks and reducing proarrhythmic risks.[7]

In conclusion, while current treatments for CPVT, such as beta-blockers, flecainide, LCSD, and ICDs, are essential, a more personalized and comprehensive approach is needed. A holistic strategy that addresses both arrhythmic and neurodevelopmental symptoms will optimize patient care. Additionally, further research into the long-term efficacy of these therapies, along with a deeper understanding of the neurodevelopmental aspects of CPVT, will be crucial in refining treatment strategies and improving patient outcomes in the future.

REFERENCES

1. Lee J, Kwon BS, Song MK, et al. Treatment outcomes in children with catecholaminergic polymorphic ventricular tachycardia: a single institutional experience. *Korean Circ J* 2024;54:853-64. CROSSREF

2. Ackerman MJ, Priori SG, Willems S, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies: this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). *Europace* 2011;13:1077-109. PUBMED | CROSSREF
3. Lieve KVV, Verhagen JMA, Wei J, et al. Linking the heart and the brain: neurodevelopmental disorders in patients with catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2019;16:220-8. PUBMED | CROSSREF
4. Yu JJ, Noh CI, Son JS, et al. Catecholaminergic polymorphic ventricular tachycardia in children. *Korean Circ J* 2000;30:191-7. CROSSREF
5. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J* 2022;43:3997-4126. PUBMED | CROSSREF
6. Roston TM, Jones K, Hawkins NM, et al. Implantable cardioverter-defibrillator use in catecholaminergic polymorphic ventricular tachycardia: a systematic review. *Heart Rhythm* 2018;15:1791-9. PUBMED | CROSSREF
7. van der Werf C, Lieve KV, Bos JM, et al. Implantable cardioverter-defibrillators in previously undiagnosed patients with catecholaminergic polymorphic ventricular tachycardia resuscitated from sudden cardiac arrest. *Eur Heart J* 2019;40:2953-61. PUBMED | CROSSREF
8. Lamba A, Roston TM, Peltenburg PJ, et al. An international multicenter cohort study on implantable cardioverter-defibrillators for the treatment of symptomatic children with catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2024;21:1767-76. PUBMED | CROSSREF