

Catecholaminergic Polymorphic Ventricular Tachycardia

Subjects: **Genetics & Heredity**

Contributor: Nicole Yin

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a condition characterized by an abnormal heart rhythm (arrhythmia).

genetic conditions

1. Introduction

As the heart rate increases in response to physical activity or emotional stress, it can trigger an abnormally fast heartbeat called ventricular tachycardia. Episodes of ventricular tachycardia can cause light-headedness, dizziness, and fainting (syncope). In people with CPVT, these episodes typically begin in childhood.

If CPVT is not recognized and treated, an episode of ventricular tachycardia may cause the heart to stop beating (cardiac arrest), leading to sudden death. Researchers suspect that CPVT may be a significant cause of sudden death in children and young adults without recognized heart abnormalities.

2. Frequency

The prevalence of CPVT is estimated to be about 1 in 10,000 people. However, the true prevalence of this condition is unknown.

3. Causes

CPVT most commonly results from mutations in two genes, *RYR2* and *CASQ2*. *RYR2* gene mutations cause about half of all cases, while mutations in the *CASQ2* gene account for up to 5 percent of cases. Mutations in other genes are rare causes of the condition.

The *RYR2* and *CASQ2* genes provide instructions for making proteins that help maintain a regular heartbeat. For the heart to beat normally, heart muscle cells called myocytes must tense (contract) and relax in a coordinated way. Both the *RYR2* and *CASQ2* proteins are involved in the movement of calcium within myocytes, which is critical for the regular contraction of these cells.

Mutations in either the *RYR2* or *CASQ2* gene disrupt the handling of calcium within myocytes, which interferes with the coordination of contraction and relaxation of the heart, particularly during exercise or emotional stress. Impaired calcium regulation in the heart can lead to ventricular tachycardia in people with CPVT.

Similarly, other genes involved in CPVT play roles in calcium regulation in myocytes. Mutations in these genes also disrupt the normal movement of calcium inside these cells, impairing the coordination of heart beats.

3.1. The Genes Associated with Catecholaminergic Polymorphic Ventricular Tachycardia

- *CASQ2*
- *RYR2*

4. Inheritance

When CPVT results from mutations in the *RYR2* gene, it follows an autosomal dominant inheritance pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In about half of cases, an affected person inherits an *RYR2* gene mutation from one affected parent. The remaining cases result from new (de novo) mutations in the *RYR2* gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

When CPVT is caused by mutations in the *CASQ2* gene, the condition almost always has an autosomal recessive pattern of inheritance. Autosomal recessive inheritance means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. Very rarely, *CASQ2*-related CPVT may follow an autosomal dominant pattern of inheritance.

When caused by mutations in other genes, CPVT can be inherited in an autosomal dominant or autosomal recessive pattern.

5. Other Names for This Condition

- bidirectional tachycardia induced by catecholamines
- catecholamine-induced polymorphic ventricular tachycardia
- CPVT
- familial polymorphic ventricular tachycardia

- FPVT

References

1. Crotti L, Spazzolini C, Tester DJ, Ghidoni A, Baruteau AE, Beckmann BM, Behr ER, Bennett JS, Bezzina CR, Bhuiyan ZA, Celiker A, Cerrone M, Dagradi F, DeFerrari GM, Etheridge SP, Fatah M, Garcia-Pavia P, Al-Ghamdi S, Hamilton RM, Al-Hassnan ZN, Horie M, Jimenez-Jaimez J, Kanter RJ, Kaski JP, Kotta MC, Lahrouchi N, Makita N, Norrish G, Odland HH, Ohno S, Papagiannis J, Parati G, Sekarski N, Tveten K, Vatta M, Webster G, Wilde AAM, Wojciak J, George AL, Ackerman MJ, Schwartz PJ. Calmodulin mutations and life-threatening cardiac arrhythmias: insights from the International Calmodulinopathy Registry. *Eur Heart J*. 2019 Sep 14;40(35):2964-2975. doi: 10.1093/eurheartj/ehz311.
2. Gomez-Hurtado N, Boczek NJ, Kryshtal DO, Johnson CN, Sun J, Nitu FR, Cornea RL, Chazin WJ, Calvert ML, Tester DJ, Ackerman MJ, Knollmann BC. Novel CPVT-Associated Calmodulin Mutation in CALM3 (CALM3-A103V) Activates Arrhythmogenic Ca Waves and Sparks. *Circ Arrhythm Electrophysiol*. 2016 Aug;9(8). pii: e004161. doi: 10.1161/CIRCEP.116.004161.
3. Leenhardt A, Denjoy I, Guicheney P. Catecholaminergic polymorphic ventricular tachycardia. *Circ Arrhythm Electrophysiol*. 2012 Oct;5(5):1044-52. doi:10.1161/CIRCEP.111.962027.
4. Lieve KV, van der Werf C, Wilde AA. Catecholaminergic Polymorphic Ventricular Tachycardia. *Circ J*. 2016 May 25;80(6):1285-91. doi: 10.1253/circj.CJ-16-0326.
5. Moscu-Gregor A, Marschall C, Müntjes C, Schönecker A, Schuessler-Hahn F, Hohendanner F, Parwani AS, Boldt LH, Ott CE, Bennewitz A, Paul T, Krause U, Rostl. Novel variants in TECRL cause recessive inherited CPVT type 3 with severe and variable clinical symptoms. *J Cardiovasc Electrophysiol*. 2020 Jun;31(6):1527-1535. doi: 10.1111/jce.14446.
6. Napolitano C, Priori SG, Bloise R. Catecholaminergic Polymorphic Ventricular Tachycardia. 2004 Oct 14 [updated 2016 Oct 13]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1289/>
7. Nyegaard M, Overgaard MT, Søndergaard MT, Vranas M, Behr ER, Hildebrandt LL, Lund J, Hedley PL, Camm AJ, Wettrell G, Fosdal I, Christiansen M, Børghlum AD. Mutations in calmodulin cause ventricular tachycardia and sudden cardiac death. *Am J Hum Genet*. 2012 Oct 5;91(4):703-12. doi: 10.1016/j.ajhg.2012.08.015.
8. Obeyesekere MN, Sy RW, Leong-Sit P, Gula LJ, Yee R, Skanes AC, Klein GJ, Krahn AD. Treatment of asymptomatic catecholaminergic polymorphic ventricular tachycardia. *Future Cardiol*. 2012 May;8(3):439-50. doi: 10.2217/fca.12.12.Review.

9. Pflaumer A, Davis AM. Guidelines for the diagnosis and management of Catecholaminergic Polymorphic Ventricular Tachycardia. *Heart Lung Circ.* 2012 Feb;21(2):96-100. doi: 10.1016/j.hlc.2011.10.008.
10. Refaat MM, Hassanieh S, Scheinman M. Catecholaminergic Polymorphic Ventricular Tachycardia. *Card Electrophysiol Clin.* 2016 Mar;8(1):233-7. doi:10.1016/j.ccep.2015.10.035. Review.
11. Roston TM, Cunningham TC, Sanatani S. Advances in the diagnosis and treatment of catecholaminergic polymorphic ventricular tachycardia. *Cardiol Young.* 2017 Jan;27(S1):S49-S56. doi: 10.1017/S1047951116002237. Review.
12. Roston TM, Van Petegem F, Sanatani S. Catecholaminergic polymorphic ventricular tachycardia: a model for genotype-specific therapy. *Curr Opin Cardiol.* 2017 Jan;32(1):78-85. Review.
13. Roux-Buisson N, Cacheux M, Fourest-Lieuvin A, Fauconnier J, Brocard J, Denjoy I, Durand P, Guicheney P, Kyndt F, Leenhardt A, Le Marec H, Lucet V, Mabo P, Probst V, Monnier N, Ray PF, Santoni E, Trémeaux P, Lacampagne A, Fauré J, Lunardi J, Marty I. Absence of triadin, a protein of the calcium release complex, is responsible for cardiac arrhythmia with sudden death in human. *Hum Mol Genet.* 2012 Jun 15;21(12):2759-67. doi: 10.1093/hmg/dds104.
14. van der Werf C, Wilde AA. Catecholaminergic polymorphic ventricular tachycardia: from bench to bedside. *Heart.* 2013 Apr;99(7):497-504. doi:10.1136/heartjnl-2012-302033.
15. van der Werf C, Zwinderman AH, Wilde AA. Therapeutic approach for patients with catecholaminergic polymorphic ventricular tachycardia: state of the art and future developments. *Europace.* 2012 Feb;14(2):175-83. doi:10.1093/europace/eur277. Dec;14(12):1810.
16. Wall JJ, Iyer RV. Catecholaminergic Polymorphic Ventricular Tachycardia. *Pediatr Emerg Care.* 2017 Jun;33(6):427-431. doi: 10.1097/PEC.0000000000001156. Review.
17. Wleklinski MJ, Kannankeril PJ, Knollmann BC. Molecular and tissue mechanisms of catecholaminergic polymorphic ventricular tachycardia. *J Physiol.* 2020 Jul;598(14):2817-2834. doi: 10.1113/JP276757.
18. Ylänen K, Poutanen T, Hiippala A, Swan H, Korppi M. Catecholaminergic polymorphic ventricular tachycardia. *Eur J Pediatr.* 2010 May;169(5):535-42. doi: 10.1007/s00431-010-1154-2.

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