

Genetics. Familial CPVT is a genetic disorder with autosomal dominant inheritance and equal male and female inheritance. The genes associated with CPVT are *RyR2* and *CASQ2*. The ryanodine receptor gene *RyR2* mutates in an autosomal dominant form of familial CPVT, this may increase sensitivity to calcium ions. The *CASQ2* inheritance is often an autosomal recessive form and encodes calsequestrin, a calcium buffering protein of the sarcoplasmic reticulum. Males with the *RyR2* mutation are at significantly higher risk than females of experiencing a cardiac event.

Families with phenotype testing results suggesting that they could be affected by CPVT should be considered for beta-blocker therapy.

Genetic analysis is now being used more more widely and is generally capable of identifying about 65% of patients with LQT, 10 to 20% of patients with Brugada, and 50 to 60% of patients with CPVT.

Definitions. The catecholamines include; epinephrine (adrenaline), norepinephrine and dopamine. They increase the heart rate, blood pressure and breathing rate.

Ventricular ectopy: a heart beat originating in the ventricle and not from the sinus node.

Phenotype: the outward physical manifestation of a genetic change.

Genotype: the internally coded inheritable (genetic) information.

References

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SADS UK played a significant role in a campaign to bring about a new chapter in the Department of Health's National Service Framework for Coronary Heart Disease. Chapter Eight, Arrhythmias and Sudden Cardiac Death was published on 4th March 2005.

The chapter includes the following recommendations for good practice for initial treatment.

Patients should receive a hard copy of their ecg which shows their arrhythmia & patients surviving cardiac arrest or having presented with pre-excited atrial fibrillation should be assessed by a heart rhythm specialist.

The following patients should be **urgently assessed** by a heart rhythm specialist:-

Patients with either syncope suggesting an arrhythmia, symptoms of arrhythmia, a personal history of structural heart disease, a family history of early sudden death, recurrent syncope with palpitations, 3rd degree AV block, or with ventricular tachycardia.

The following should be **referred** to a heart rhythm specialist:-

People with suspected ventricular tachycardia, patients with WPW Syndrome, recurrent SVT not controlled by medication, recurrent atrial flutter, symptomatic atrial fibrillation not controlled by medication, first degree relatives of victims of sudden cardiac death who died below the age of 40 years, or patients with inexplicable recurrent falls.

The Recommendations for Ongoing Treatment are:-

Patients with sustained or compromising arrhythmias receive timely referral for appropriate treatment. Those identified at being high risk or with life-threatening ventricular arrhythmias should be considered a candidate for an implantable cardioverter defibrillator (ICD). For patients with sustained SVT catheter ablation should be considered. An outpatient care plan is devised between patient, GP and arrhythmia care team, when further hospital treatment is not recommended.

For full details see Department of Health website:
<http://www.dh.gov.uk/assetRoot/04/10/52/80/04105280.pdf>

Please make a donation to SADS UK to enable us to support those affected by cardiac arrhythmia and sudden cardiac death –

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Grateful thanks to Dr Andrew Grace for helping compile this leaflet



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The heart beat. The heart is a strong muscle that pumps blood around the body when its chambers expand and contract. The heart is divided into four chambers, the upper chambers are called the atria and the lower chambers the ventricles. The weaker atria chambers fill the ventricles with blood, these two stronger chambers then contract pumping the blood around the body. The right side of the heart pumps blood to the lungs to enrich it with oxygen; the left chambers then pump the oxygen rich blood to the brain and the rest of the body.

The heart has its own electrical system that controls each heart beat (contraction). When the heart is pumping normally, the beat (depolarisation) starts from the sinus node which is located in the right atrium. It then passes through the atrioventricular node, along the His bundle (conduction pathway) and its branches to the ventricles. As the electrical impulse travels through the bundle branches and over the ventricles, it causes the muscle to contract. This contraction forces the ventricles to pump blood around the body. The sinus node is referred to as the heart's natural pacemaker as it controls the heart rate.

What is CPVT? CPVT is an inherited disease that causes cardiac arrhythmias due to an electrical instability in the hearts pacing system described above. There is no apparent physical problem with the heart muscle.

The origin of the CPVT arrhythmia is considered to be in the right ventricle where QRS morphology (ECG pattern) shows a left bundle branch block pattern, and in the left ventricle when a right bundle branch block pattern is present. The electrical signal that causes the onset of CPVT is mostly single or double origin and usually originates from the right ventricular outflow tract instead of at the sinus node. The following beat tends to originate from within the left ventricle.

CPVT is usually characterised by bidirectional polymorphic VT that can be induced during exercise or catecholamine infusion and other events provoking sympathetic nervous system activation. A third of patients suffering from CPVT have a family history of premature sudden death or stress-related syncope.

The symptoms of CPVT include; exercise-induced polymorphic ventricular arrhythmias, syncope occurring during physical activity or acute emotion.

Without treatment a patient with CPVT is prone to ventricular tachycardia (VT), this may self terminate or degenerate to ventricular fibrillation which can in some cases cause sudden death.

Who is affected. The CPVT arrhythmias may affect significantly less people than other arrhythmic disorders such as the LQT syndrome although the spectrum may expand. CPVT is thought to affect approximately 1 in 10,000 people whereas LQT affects approximately 1 in 5,000 people. The number affected may be higher than this however.

The majority of people affected by CPVT may experience episodes of ventricular tachycardia in childhood and adolescence, 60% of patients have their first episode of syncope before the age of 20 years. Childhood and adolescence are normally when individuals are most active, where sporting and other strenuous activities are more likely to induce the CPVT arrhythmias. A mutation in the ryanodine receptor (*RyR2*) or Calsequestrin-2 (*CASQ-2*) genes are associated with CPVT in around 60% of those affected.

The first syncope event will generally occur in males much earlier than in females. In 30% of families affected by CPVT there is likely to be a history of sudden death. In 60% to 70% of the individuals affected by CPVT there will be a history of syncope. Sudden death may result from having a CPVT episode but the incidence of sudden death may be rare.

Diagnosis and testing. Symptoms are palpitations, dizziness and syncope occurring during physical activity or acute emotion.

It is not practical to make a diagnosis of CPVT with a standard 12 lead ECG recording taken at rest, an ECG test is required where the patient is undertaking exercise or under some other stress. The exercise is gradually increased in severity to see if ventricular tachycardia can be induced. As the exercise severity continues to be increased the VT may become sustained.

Adrenaline infusion through a peripheral intravenous line with ECG monitoring may also be used to help unmask ventricular arrhythmia. The use of Adrenaline may cause polymorphic ventricular ectopy, nonsustained ventricular tachycardia or frequent ventricular ectopy. Studies suggest that Adrenaline can be more effective at unmasking evidence of CPVT in patients than by using exercise testing. The number of patients that have positive adrenaline tests may be higher than has been thought and this is an area of active research.

An alternating 180 degree change of the QRS (see labelling of the heart beat on the ECG trace) axis on a beat to beat basis, so called bi-directional VT is the usual ECG manifestation. The changes in QRS waveform will be abrupt which is very different to the *torsade de pointes* noted in LQT syndrome. The QRS waveform will be regular not chaotic.

All first degree relatives of a patient with CPVT should be tested to see if they have symptoms of the disease. Checkups every 6 to 12 months with an exercise test at the maximum heart rate for the individual's age is recommended in selected cases.

Treatment: Beta-blocker therapy is an effective treatment for approximately 60% of patients with CPVT. The correct dosage is guided by exercise testing. In some cases, taking beta-blockers alone may not be effective enough, it may still be possible to provoke the arrhythmias at high heart rates, in these cases the patient should be considered for an ICD.

The beta-blocker used should block both beta 1 and beta 2 receptors in the heart and therefore typically either propranolol or nadolol are used. Some so-called selective beta-blockers may be hazardous in this condition.

High risk patients are those with recurrent syncope and who may have survived a cardiac arrest. High risk patients would benefit from an ICD being fitted, along with the beta-blocker treatment.

Antiarrhythmic drugs such as amiodarone, sodium channel blockers and calcium antagonists appear ineffective in providing effective arrhythmia suppression for CPVT.

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The primary purpose of this leaflet is for guidance;
specialist advice should be sought regarding.

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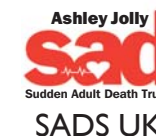
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