Supplement

Ventricular Tachycardia in Structurally Normal Hearts: Recognition and Management

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Abstract

Idiopathic ventricular tachycardia is a defined set of tachycardias when structural or pathological cause has been ruled out for the same. This paper tries to define and classify these arrhythmias to organize a logical therapeutic approach to deal with them. 60-80% of the idiopathic tachycardias originate from the right ventricular outflow tract (RVOT) and in 10% from the left ventricular outflow tract (LVOT). Outflow tract tachycardias have either LBBB or RBBB morphology with early R wave transition in chest leads. Adenosine, beta blockers and calcium channel blockers is the common medical treatment. Radiofrequency ablation is however the treatment of choice. Verapamil sensitive left ventricular tachycardia (ILVT) and propranolol sensitive left ventricular tachycardia (IPVT) are the other two forms recognized. RF ablation seems ideal for long-term management of ILVT and implantable cardioverter defibrillator (ICD) for IPVT. Inherited channelopathies include catecholaminergic polymorphic ventricular tachycardia (CPVT), Brugada syndrome and long QT syndrome where there is an inherited disorder in the ion-exchange channels of the cell-membrane leading to tachycardia. Prognosis in these is variable; CPVT, in particular, has a malignant course when untreated. RF ablation and placement of an ICD are important in the overall management of specific arrhythmia.

Ventricular tachycardia occurring in an otherwise structurally normal heart is defined as idiopathic ventricular tachycardia. Structural heart disease can be ruled out if the ECG (except in Brugada syndrome and long QT syndrome), echocardiogram, and coronary arteriogram collectively are normal. However, MRI can detect these structural abnormalities in the presence of all other imaging diagnostic techniques being normal, especially in cases of right ventricular outflow tract tachycardia (RVOT VT). Also, single-photon emission computed tomographic scans (SPECT) detect cardiac innervation abnormalities, which is seen in such structurally normal hearts with ventricular arrhythmias. Electropharmacologic data suggests that multiple arrhythmogenic mechanisms may account for these arrhythmias.

The classification of idiopathic ventricular tachycardia has been with respect to ventricle of origin, response to pharmacologic agents, evidence of catecholamine dependence and specific morphologic features of arrhythmia (QRS morphology, axis, pattern, and whether tachycardia is repetitive, non-sustained, or sustained) (Table 1). Thus following types of VT occur in the absence of structural heart disease: a) right ventricular outflow tract (RVOT) VT, b) idiopathic left ventricular tachycardia (ILVT), c) idiopathic propranolol sensitive VT (IPVT), d) left ventricular outflow tract (LVOT) VT, e) catecholaminergic polymorphic VT (CPVT), f) Brugada syndrome and g) long QT syndrome (LQTS). RVOT VT, ILVT, IPVT generally do not have a familial basis. RVOT VT and ILVT are monomorphic, whereas IPVT may be monomorphic or polymorphic. CPVT, Brugada syndrome and LQTS are inherited ion-channelopathies. CPVT may present as bidirectional VT, polymorphic VT, or catecholaminergic ventricular fibrillation. Syncope and sudden death in Brugada syndrome are usually due to polymorphic VT. The characteristic arrhythmia of LQTS is Torsades de Pointes. RVOT VT, ILVT, IPVT, LVOT VT are referred to as idiopathic VT and have a better prognosis. Prognosis for patients with VT secondary to ion-channelopathies is variable. Thus as is evident there can be no watertight classification of idiopathic ventricular tachycardias (Fig. 1) (Table 1).

OuTfLOw TRAcT VeNTRicuLAR TAcHYcARdiA

RV monomorphic extra systoles are considered benign. However, they may progress to arrhythmogenic right ventricular dysplasia and RVOT VT, with the MRI showing anatomical and functional abnormalities of the right ventricle. These extra systoles have an LBBB morphology on ECG with the QRS axis directed inferiorly. Long-term follow up of these RV monomorphic extrasystoles showed that none of the patients died of sudden death or developed right ventricular dysplasia. However focal fatty replacement in the right ventricle was seen in most.

80-90% of the tachycardias in normal hearts originate from the RVOT and 10% from the LVOT. RVOT VT is seen more commonly in females in 30-50 years of age. Most patients present with palpitations or presyncpe but rarely present with frank syncpe. Exercise or emotional stress usually precipitates the tachycardia. Sudden death is rare. The characteristic morphology of RVOT VT is a wide QRS complex tachycardia with LBBB pattern and an inferior
The most common feature of this tachycardia is verapamil sensitivity. Seen in second to fourth decade of life and occurs more often in men (60%-80%).

ILVT: IDIOPATHIC LEFT VENTRICULAR TACHYCARDIA

The hallmark of ILVT is that it is not inducible with programmed electrical stimulation, but isoproterenol infusion usually induces this VT and beta-blockers are effective in completely terminating the tachycardia.

Treatment of ILVT

Pharmacologic therapy with verapamil is still the treatment of choice for ILVT because of a good long-term prognosis. RF ablation is effective and safe with no complication recorded. After ablation of the clinical VT, 11% of subjects showed a recurrence of both ILVT and RVOT VT with a different morphology in a study which was successfully reablated. Low energy DC shocks can be safely used when RF ablation proves ineffective.

IPVT: IDIOPATHIC PROPRANOLOL SENSITIVE VENTRICULAR TACHYCARDIA

This is also a form of idiopathic left ventricular tachycardia. The hallmark of IPVT is that it is not inducible with programmed electrical stimulation, but isoproterenol infusion usually induces this VT and beta-blockers are effective in completely terminating the tachycardia.

Treatment of IPVT

Beta-blockers are used to treat this form of VT because they are effective in acute situations. This type of VT is unresponsive to verapamil. Long-term management of IPVT has not been studied in details, however cardioverter-defibrillator (ICD) may be implanted in patients who survive sudden cardiac death.

INHERITED CHANNELOPATHIES

CPVT: Catecholaminergic Polymorphic Ventricular Tachycardia

CPVT is an inherited disorder characterized by a bidirectional polymorphic VT. This type of arrhythmia is induced by exercise or emotion or any form of increased adrenergic stimulation. 30% of the patients have a family history of sudden death or syncope. CPVT is an important cause of sudden death and syncope in children with normal heart. Since the tachycardia resembles the arrhythmia associated with calcium overload, the abnormality was traced to the mutation in the RyR2 gene which is important for the regulation of intracellular calcium fluxes. The non genotyped CPVT patients became symptomatic at a younger age than the non genotyped CPVT patients, thus suggesting males at a higher risk for syncope due to RyR2CPVT. The RyR2CPVT patients became symptomatic at a younger age than the non genotyped CPVT patients, thus suggesting males at a higher risk for syncope due to RyR2CPVT. The RyR2CPVT patients became symptomatic at a younger age than the non genotyped CPVT patients, thus suggesting males at a higher risk for syncope due to RyR2CPVT.
because of symptomatic recurrence of life-threatening arrhythmia in spite of beta-blocker therapy. 

**BRUGADA SYNDROME**

First reported by Brugada et al, this abnormality is characterized by RBBB pattern (early high take-off of the ST segment but absence of wide S wave in left lateral leads which rules out a true RBBB), ST elevation in right precordial leads (V1-V3), normal QT interval, absence of structural heart disease, life-threatening cardiac arrhythmia (polymorphic VT) and a family history of sudden death. Two types of ST elevation have been described: coved and saddleback. The coved type has been shown to have a greater potential to cause arrhythmia than the saddleback type. A mutation in the cardiac sodium channel gene (SCN5A) has been described in this syndrome. The electrocardiographic manifestations of the Brugada syndrome can be unmasked using sodium channel blockers such as flecainide, ajmaline or procainamide which further supports the sodium channel abnormality. The signal averaged ECGs showing late potential has been shown to be most useful in identifying high risk patients for Brugada syndrome. The clinical presentation in Brugada syndrome was studied and showed that VF was present in 76 (73%) and syncope in 28 (27%) of the patients. (The Brugada-type ECG (“Brugada sign”) may be much more common than is the clinical syndrome. The risk of sudden cardiac death due to polymorphic VT or ventricular fibrillation with Brugada syndrome is substantial.

**Treatment of Brugada Syndrome**

There is no effective drug treatment. Quinidine has shown to have normalizing effect on the ECG of patients showing Brugada pattern of ECG, thus proving some scope for Class Ia anti-arrhythmic in this syndrome. In symptomatic patients, ICD placement is the treatment of choice. Asymptomatic patients with Brugada-type ECG results should undergo electrophysiologic testing. If ventricular arrhythmia is inducible the patient should receive an ICD. Asymptomatic patients with normal baseline ECG do not require further testing.

**LQTS –LONG QT SYNDROME**

LQTS is an uncommon disorder due to mutations in 7 genes (Table 2).

Some investigators have classified Andersen syndrome (AS) a rare, inherited disorder characterized by periodic paralysis, long QT (LQT) with ventricular arrhythmias and skeletal developmental abnormalities as a form of LQTS (LQT7).

Individuals with LQTS and deafness (Jervell Lange-Neilsen syndrome) have the highest risk for experiencing life threatening arrhythmias. The most common clinical presentation is syncope or sudden cardiac death, triggered by exercise (LQT1) and acute arousal such as sudden loud noise (LQT2). Sudden death can occur at rest or during sleep (LQT3). Priori et al conducted a study on 647 LQTS patients and found that the risk of cardiac events is higher in LQT2 and LQT3 as compared to LQT1. Gender had no influence across most genotypes. However, there was greater risk for LQT2 in females and LQT3 in males. Asymptomatic (“silent carriers”) were also highest in LQT1 than in LQT2 and LQT3.

Typical ECG patterns have been defined for various genotypes of long-QT. LQT1 showing a broad based, peaked or late onset-T wave; LQT2 showing bifid T wave; LQT3 showing a late-onset, peaked or biphasic T wave; making a diagnosis of LQTS likely. Family history may be helpful for diagnosis of LQTS. Recurrence of a clinical event is quite frequent in LQTS.

**Treatment of LQTS**

Adrenergic modulation with beta-blockers is the most useful therapy since 1970 in both symptomatic and asymptomatic patients. The number of patients with cardiac events was significantly reduced after the initiation of beta-blocker therapy (preferably non-selective beta-blockers). However the study showed that it does not absolutely prevent death. Also patient compliance was an issue. Pacemakers can be used when sinus bradycardia and sinus pauses become exacerbated. Surgical sympathectomy is an adjuvant treatment but is now done rarely. Oral potassium may be useful in certain genotypes. ICD placement, along with beta-blocker therapy, offers the best protection in high-risk patients (survivors of sudden death and those with recurrent syncope).

Medications that prolong QT interval must be carefully excluded from the patient’s medication list.

**Drug induced QT prolongation and Torsades de Pointes**

![ECG 1: Long QT syndrome (LQTS), best seen in V2, V3, maybe missed in other leads.](image1)

![ECG 2: Torsades de pointes (TdP) starting with a VPB on the descending limb of the previous T wave.](image2)

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**Table 2: Classification of the genes responsible for LQTS**

<table>
<thead>
<tr>
<th>LQTS subtype</th>
<th>Mutated gene</th>
<th>Ionic current affected</th>
<th>Clinical frequency, %</th>
<th>Trigger of clinical event</th>
</tr>
</thead>
<tbody>
<tr>
<td>LQT1↑</td>
<td>KCNQ1</td>
<td>Slow activating potassium current</td>
<td>44-54</td>
<td>Conditions of increased sympathetic activity, exercise, swimming</td>
</tr>
<tr>
<td>LQT2</td>
<td>HERG</td>
<td>Rapid activating potassium current</td>
<td>53-35</td>
<td>Sudden arousal, emotions, auditory stimuli-loud noises</td>
</tr>
<tr>
<td>LQT3</td>
<td>SCN5A</td>
<td>Activating sodium current</td>
<td>6-11</td>
<td>Sleep, night-time</td>
</tr>
<tr>
<td>LQT4</td>
<td>Ankyrin B</td>
<td>Sodium pump, sodium/calcium exchanger and inositol receptors</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>LQT5↑</td>
<td>KCNE1 (minK)</td>
<td>Slow activating potassium current</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>LQT6</td>
<td>KCNE2 (MiRP1)</td>
<td>Rapid activating potassium current</td>
<td>Rare</td>
<td></td>
</tr>
</tbody>
</table>
Torsades de pointes (TdP) is a form of polymorphic ventricular tachycardia where the QRS axis seems to twist around an imaginary baseline. QT prolongation represents delayed repolarisation which can lead to TdP. Acquired QT prolongation is mostly due to medication. Anti arrhythmic drugs have known QT prolonging effects, however recently non-cardiac drugs like terfenadine and cisapride and certain antipsychotic drugs have also shown positive QT prolongation in drug trials on healthy volunteers. Immediate action for drug induced QT prolongation is to suppress the tachyarrhythmia. Intravenous magnesium sulphate has been shown to be useful. In a study conducted among US adults, the results showed that female sex, hypocalcemia (men), hypokalemia (women), a history of thyroid disease and myocardial infarction (men) were associated with a prolonged QTc interval. In addition, taking QT-prolonging medications in the past month was associated with more than a twofold increase in the odds of prolonged QTc interval in both men and women (Fig. 2).

REFERENCES

Fig. 2: Diagnostic approach to ventricular arrhythmia in the absence of structural heart disease.


