Premature Ventricular Contractions (PVCs)

When to Refer for Ablation

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• 31 year old female with 4 year history of palpitations and skipped beats that have become very frequent and interfering with her usual activities. ECG during symptoms showed frequent PVCs. Otherwise she has no significant medical history and never had sustained tachycardia.

• Echo showed normal LVF with LVEF=55%. Normal dimensions

• ETT: PVCs decreased during exercise and increased during recovery

• She was placed on Verapamil and then Bisoprolol 5 mg daily without significant improvement.

• 24 hour holter monitor showed 34% PVCs with single morphology

**You would:**

Reassure, continue beta blocker therapy

Start Flecainide

Start Amiodarone

Refer for ablation
Incidence, Prevalence, and Prognosis

PVCs are present on ECG in 1% of apparently healthy subjects and in 40-75% in a 24-48 hour holter monitors.

Prevalence is increase by age (so is heart disease). Less than 1% in children to almost 70% in subjects over 75 years old.

Relatively benign in patients with no structural heart disease. But not always ......
Prognosis of asymptomatic ventricular arrhythmias in apparently healthy adults

The Framingham Heart Study:
The presence of complex ventricular arrhythmias was associated with a two-fold increase in the risk for all-cause mortality and myocardial infarction or death due to coronary heart disease.

The Copenhagen Holter Study:
The detection of frequent PVCs was an independent predictor of cardiovascular events (hazard ratio 2.6).

Multiple Risk Factor Intervention Trial (MRFIT):
The finding of any VPCs on a 2-min rhythm strip was independently associated with a threefold increase in sudden cardiac death at seven year follow-up.
Kennedy et al. No increase in all-cause mortality or myocardial infarction or death from coronary heart disease in people without coronary heart disease who had complex or frequent arrhythmias

In a study of 239 people with frequent PVCs and no structural heart disease there was no serious cardiac events at 5.6 years follow-up, but there was correlation between PVC prevalence and decrease of ejection fraction and increase of left ventricular diastolic dimension.

Meta-analysis of 11 studies, people with frequent PVC had risk of cardiac death two times higher than persons without frequent PVC.

The conflicting results were thought to be due to how vigorous the work up to rule out underlying heart disease between the different studies.
PVCs in Patients without overt Structural heart disease

- Majority originate from the ventricular outflow tract with the RVOT being the most common location (70%)

- Other locations include: Aortic sinuses of Valsalva (20%), LVOT, great cardiac veins, epicardial myocardium, aorta-mitral continuity or, papillary muscles

- No SHD but some abnormalities have been seen by CMR in some patients

- Mechanism is focal: Mainly Delayed afterdepolarizations and triggered activity. micro-reentry, or automaticity also have been proposed
Ventricular Arrhythmias (Outflow tract PVCs and VT) in Patients without overt Structural heart disease

• Benign course. However, malignant form is seen rarely.

• Monomorphic, and has long coupling interval to the preceding QRS complex.

• Exercise / stress induced or repetitive MMVT at rest

• Exercise induced PVCs triples the mortality at 12 months compared to PVCs at rest

• Multiple morphologies should raise the suspicion of scar related VT like in ARVC

• **Can be a cause of tachycardia mediated cardiomyopathy when they are very frequent**
PVC induced Cardiomyopathy

Suppression of frequent premature ventricular contractions and improvement of left ventricular function in patients with presumed idiopathic dilated cardiomyopathy.

Duffee DF, Shen WK, Smith HC.

OBJECTIVE: To examine the hypothesis that suppression of frequent premature ventricular contractions may be associated with improvement in left ventricular function in patients with presumed idiopathic dilated cardiomyopathy.

DESIGN: We conducted a retrospective case study and statistical analysis of the effect of cardiac medical therapy on outcome.

MATERIAL AND METHODS: The study population consisted of 14 patients with more than 20,000 premature ventricular contractions in 24 hours recorded by Holter monitoring and associated left ventricular dysfunction (ejection fraction, 40% or less). Clinical characteristics, number of premature ventricular contractions per hour on 24-hour ambulatory Holter monitoring, and ejection fraction based on transthoracic echocardiography were compared before and after cardiac therapeutic intervention.

RESULTS: Of the 14 patients, 10 had presumed idiopathic dilated cardiomyopathy, and 4 had ischemic heart disease. Of the overall study group, seven had received additional cardiac medical therapy after the index evaluation, including four patients who had amiodarone therapy. A significant reduction (75% or more from baseline) in premature ventricular contractions after medical therapeutic intervention was observed in five patients at the first follow-up examination. The mean interval to the first follow-up examination was 6 +/- 3 months. Of the five patients, four had significant improvement in clinical functional status and the ejection fraction. The mean ejection fraction of these five patients increased from 27 +/- 10% at baseline to 49 +/- 17% after medical therapy (P = 0.04).

CONCLUSION: The suppression of frequent premature ventricular contractions may be associated with improvement of left ventricular function in patients with presumed idiopathic dilated cardiomyopathy.

PVC induced Cardiomyopathy

Ventricular ectopy as a predictor of heart failure and death

*Dukes et.al. J. Am Coll Cardiol. 2015 Jul 14; 66(2): 101-109*

- Population based observational trial
- 1139 healthy objects (no heart disease). Mean F/U over 13 years
- **Frequent PVCs were associated with**
  - 3-fold greater odds of a 5-year decline in LVEF (OR: 3.10, 95%CI: 1.42 to 6.77, p=0.005)
  - 48% increase risk for CHF (HR:1.48, 95%CI: 1.08 to 2.04, p=0.02)
  - 31% increased risk of death (HR1.31, 95%CI: 1.06 to 1.63, p=0.01)
PVC Induced Cardiomyopathy

The majority of patients with frequent PVCs will not develop LV dysfunction but some will.....

PVC burden is the most important predictor with the cut-off ranging from 10 - 26%

24% Burden:
80% sensitivity and specificity

16% Burden: sensitivity 90% and 58% specificity
PVCs Induced Cardiomyopathy

The pathogenesis of PVC-mediated cardiomyopathy is uncertain.

**Possible hypotheses include:**
- Ventricular dyssynchrony
- Hemodynamic impairment
- Increased oxygen demand
- Autonomic dysregulation
- Alterations in intracellular calcium handling
- Altered heart rate dynamics

Animal models showed no inflammation, fibrosis or apoptosis suggesting possible functional abnormalities
PVCs Induced Cardiomyopathy

Improvement of LV Function after Catheter ablation

174 patients referred for ablation of frequent PVCs. A reduced LVEF (37±10%) was present in 57/174 patients (33%). Among the patients with LV dysfunction before ablation, EF normalized or increased by >15% in 46/57 (81%) a mean of 3.6 months after ablation. The lowest PVC burden resulting in reversible cardiomyopathy was 10%.
Multicenter Outcomes for Catheter Ablation of Idiopathic Premature Ventricular Complexes
Latchamsetty et.al. JACC June 2015

Retrospective study, 1185 pts.
Mean EF=55%±10%
Mean PVC burden 20+13%

Acute success rate: 84%

- Right ventricular outflow tract (RVOT) location was predictive of acute procedural success
- Epicardial location and increasing premature ventricular complex (PVC) configurations were predictive of failure
Radiofrequency Ablation Versus Antiarrhythmic Medication for Treatment of Ventricular Premature Beats From the Right Ventricular Outflow Tract


Prospective randomized study
330 pts.
Catheter ablation vs. AA drugs

Catheter ablation was more effective in:
- Reducing recurrences of PVCs (19.4 vs. 88.6)
- Reducing burden of PVCs
Catheter Ablation of PVCs

• No Large prospective randomized multicenter clinical trials

• Available studies enrolled markedly symptomatic patients with high PVC burden

• Success rate: 75-100%. Complication rate 1-3%

• Procedural success is dependent on:
  • Site of origin (RVOT vs. LVOT vs. epicardial ....)
  • Single or multiple morphologies
  • Ability to induce the clinical PVC
  • The use of advances mapping systems
# PVCs and Cardiomyopathy: The Chicken or the Egg?

<table>
<thead>
<tr>
<th></th>
<th>PVCs resulting from CM</th>
<th>PVCs causing CM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td>Older, known CV disease</td>
<td>Healthy</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td>CAD, HTN, DM, myocarditis</td>
<td>None relevant for CM</td>
</tr>
<tr>
<td><strong>PVC frequency</strong></td>
<td>Less than 5000/24 hours</td>
<td>Over 10,000/24 hours (over 20%)</td>
</tr>
<tr>
<td><strong>PVC pattern</strong></td>
<td>Multi-morphic</td>
<td>Monomorphic</td>
</tr>
<tr>
<td><strong>PVC (QRS) morphology</strong></td>
<td>Non-specific</td>
<td>Suggestive of a single specific focus (OFT, fascicular)</td>
</tr>
<tr>
<td><strong>PVC suppression with drug therapy or ablation</strong></td>
<td>No improvement in LV function</td>
<td>Improvement in LV function</td>
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</table>
PVCs in Patients without Apparent Structural heart disease
Evaluation and work-up

The extent of work up depends on clinical history

• Age
• Associated symptoms (syncope)
• Family history
• Morphology and frequency of PVCs

• **Is there underlying structural heart disease or channelopathy?**
  • CAD and ischemia, HCM, ARVC, CPVT, Brugada, long or short QT syndrom
PVCs in Patients without Apparent Structural heart disease Evaluation and work-up

- **ECG:** MI, ischemia, LVH, ARVC, Brugada, and other channelopathies...
- **Laboratory data** (electrolytes...)
- **Holter monitor:** Morphology and burden of PVCs
- **Event monitors and loop recorders**
- **Echocardiogram:** Structural heart abnormalities
- **Exercise test (ETT):** Ischemia or exercise induced PVCs and VT
- **CMR:** When structural abnormalities still suspected (echo was inadequate)
- **Cardiac catheterization:** to assess for significant CAD when indicated
## Treatment of Outflow Tract Ventricular Arrhythmias

**ESC Guidelines 2015**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
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<tbody>
<tr>
<td>Catheter ablation of RVOT VT/PVC is recommended in symptomatic patients and/or in patients with a failure of anti-arrhythmic drug therapy (e.g. beta-blocker) or in patients with a decline in LV function due to RVOT-PVC burden.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Treatment with sodium channel blockers (class IC agents) is recommended in LVOT/aortic cusp/epicardial VT/PVC symptomatic patients.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Catheter ablation of LVOT/aortic cusp/epicardial VT/PVC by experienced operators after failure of one or more sodium channel blockers (class IC agents) or in patients not wanting long-term anti-arrhythmic drug therapy should be considered in symptomatic patients.</td>
<td>IIA</td>
<td>B</td>
</tr>
</tbody>
</table>
Frequent and complex PVCs in patients with structural heart disease and/or LV dysfunction

Independent risk factor for increased mortality and SCD in pts with LV dysfunction
May cause further reduction in left ventricular systolic function and worsening symptoms
Optimization of therapy for the type of structural heart disease and ICDs when indicated as per guidelines
Beta blockers are indicated in pts with LV dysfunction. Amiodarone (CHF-STAT trial: 80% Reduction in PVC burden in 69% of patients with improvement in LV function but has side effects and discontinuation rate of 27%) or ablation will reduce the burden of PVCs. However, class Ic drugs are contraindicated because of proarrhythmic effects and increased mortality
PVC reduction (by drugs or ablation) in CRT patients with frequent PVCs will improve % of biventricular pacing and clinical response
When LV dysfunction is thought to be due to high PVC burden and no other identifiable causes, it is reasonable to ablate the PVCs and reassess LV function in 3-6 months before considering device therapy.
Outflow track anatomy:

The Pulmonary artery is anterior and to the left.

The ascending aorta is posterior and to the right.

The pulmonic valve is superior to the aortic valve.

Most anterior structure: Free wall or anterior RVOT

Anterior part of aortic supra-valvular region is adjacent to posterior RVOT.

RVOT may be crescent shaped: The posteroseptal region directed rightward and the anteroseptal region directed leftward.
Outflow track PVC origin:

LBBB with inferior axis (QRS positive in II, III, aVF)
All outflow tachycardias have negative aVR and aVL (QS)
A small R or isoelectric in aVL: Near HIS location

**In V1:**

No R: Anterior RVOT location.

A small initial R: Posterior RVOT or right coronary cusp of the aorta

A more prominent R: Left coronary cusp of the aorta (or AMC, NCC)

A RBBB morphology: Mitral annulus
Outflow track PVC origin:

**RVOT vs LVOT:** PreCORDial leads transition:
- Late transition (after V3): RVOT
- Early transition: (before V3): LVOT, coronary cusps

**Free wall vs Septum:** Leads II, III, aVF
- Free Wall: Notching. QRS over 140ms
- Septum: Narrower QRS, no notching

**Anterior vs posterior:** Lead I
- Anterior (site 3): Negative
- Posterior (site 1): Positive
Epicardial origin of the PVC

• **Pericordial MDI over 0.55**

• MDI: Maximum deflection index

• TMD: Time to maximum deflection is a precordial lead

• **Epicardial origin: Wider QRS with significant initial slurring**
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Refer for ablation
VT Induced during EP study
LCC origin of the PVC
Post PVC ablation
Pace Mapping (12/12 match)

Pacing at the site of early activation

The clinical PVC
Early activation at site of PVC ablation (antero-septal location)

Elimination of PVC during ablation
**Short coupled PVCs and Ventricular Fibrillation**

Rare

PVCs originating from the RVOT with short coupling interval (less than 300ms) initiating PMVT and VF

Compared to patients with the benign form of RVOT PVCs:
- More syncope
- Shorter cycle length
- Wider PVC QRS complex

Management: ICD for secondary prevention. Ablation targeting the initiating PVC
Summary

• Adequate evaluation and workup should be done to assess for the presence of undiagnosed structural heart disease or conditions that could increase the risk for malignant ventricular arrhythmias (channelopathies...)

• Asymptomatic or mildly symptomatic patients with infrequent PVCs, couplets, or triplets do not require specific drug therapy.

• Asymptomatic or mildly symptomatic patients with frequent PVCs (over 10,000 per day): Longitudinal follow-up with echo to detect development of LV dysfunction or increased in chamber volume

• In symptomatic patients: BB or non-dihydropyridine CCB. Anti-arrhythmic drugs (Flecainide, sotalol, propafenone, mexiletine, amiodarone....) can be used if BB or CCB are ineffective in the absence of significant heart disease

• Catheter ablation improves symptoms in highly symptomatic patients with frequent PVCs (over 10,000 per day) and can reverse LV dysfunction

• No evidence yet for catheter ablation of frequent asymptomatic PVCs to prevent the development of LV dysfunction.