Premature Ventricular Contractions

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Disclosures

• Under Accreditation Council for Continuing Medical Education guidelines, disclosure must be made regarding financial relationships with commercial interests within the last 12 months

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• I have no relevant financial relationships or affiliations with commercial interests to disclose
Outline

• Case
• Prevalence
• Mechanism
• Associated conditions
• Clinical presentation
• Evaluation
• Prognosis
Case

• 68yo WM with CAD s/p inferior MI c/b ischemic cardiomyopathy (EF 45%), RBBB, PVCs, NSVT presented with frequent PVCs and symptoms of fatigue and shortness of breath

• No syncope, presyncope

• Holter: 36,000 PVCs (30%), periods of bigeminy, trigeminy and NSVT

• Intolerant to beta-blockers
Prevalence

• Duration of monitoring

• 1% on 12 lead ECG
• 80% on 24 hour holter monitor
Mechanism

- Re-entry
- Enhanced normal or abnormal automaticity
- Triggered activity
Associated Conditions

- Hypertension with LVH
- Acute myocardial infarction
- Heart failure
- Hypertrophic cardiomyopathy
- Congenital heart disease
- Idiopathic ventricular tachycardia
- Other: OSA, COPD, pHTN, stimulants, endocrinopathies
Clinical Presentation

- Asymptomatic
- Palpitations, lightheadedness
- Anxiety
- Palpitations $\rightarrow$ anxiety $\rightarrow$ catecholamine surge $\rightarrow$ ectopy $\rightarrow$ anxiety
- Reversible cardiomyopathy
Evaluation

- History, exam
- 12 lead ECG
- Ambulatory monitoring
- Transthoracic echocardiogram
- Exercise treadmill stress test
- ? Electrolytes, OSA screening, UDS
Electrocardiography

- QRS duration > 120 msec
- Bizarre morphology (not typical aberration)
- T wave in opposite direction of main QRS
- Fully compensatory pause
RVOT PVCs
Prognosis in “Normal Hearts”

- ARIC $\Rightarrow$ single PVC on 2 minute ECG had 2 fold increase in mortality from CHD
- ARIC $\Rightarrow$ 2 fold increase in sudden cardiac death
- Meta-analysis 8 prospective studies (3,629 persons) PVC was associated with increased all cause mortality, cardiovascular mortality, SCD, or ischemic CHD (OR 1.72, 95% CI 1.28-2.31)
- Meta-analysis 106,195 persons $\Rightarrow$ 1 PVC on 10 second ECG or >30 in 1 hour recording associated with overall cardiac mortality (RR 2.1, 95% CI 1.7-2.5) and SCD
- Several cohort studies report no clinical significance
Exercise

- Withdrawal of vagal tone
- Sympathetic stimulation $\rightarrow$ increased circulating catecholamines
- Increased HR, AV conduction, contractility
- Increased cardiac output and oxygen delivery
- Initiate abnormal automaticity, triggered activity, re-entry
Cellular Mechanisms

Diagram showing the interaction between various cellular mechanisms, including G-protein signaling pathways, calcium channels, and the effects of antagonists and agonists on cellular activity.
Specific Conditions

• Exercise

• Structural heart disease

• Myocardial infarction

• CHF
Ventricular arrhythmia during exercise predicts an increased cardiac mortality

Among 6101 normal men who underwent exercise testing and were followed for 23 years, the occurrence of ventricular premature beats (VPBs) during exercise testing was associated with a significantly higher all-cause mortality (41 versus 26 percent for no VPBs) and death from cardiovascular disease (16 versus 6.4 percent). After adjusting for age, tobacco use, diabetic status, body-mass index, level of physical activity, systolic blood pressure, the heart rate at rest, and total cholesterol level the presence of VPBs prior to or during exercise was an independent predictor of cardiovascular mortality (relative risk 2.53) and had the same prognostic value as exercise induced ischemia (relative risk 2.63).

Catecholaminergic PVT

- Inherited disorder
- Syncope, sudden death
- Presents in children and teenagers
- Structurally normal heart
- Normal ECG
- VT elicited by physical and emotional stress
- Bidirectional ventricular tachycardia
- Syncope or cardiac arrest before 40
- Beta-blockers, ICD
Bidirectional VT
Acute MI

- PVCs are seen in the majority of MIs
- <48 hours → do not appear to affect prognosis
- Conflicting data after 48 hours
- PVCs carry a worse prognosis
CHF

• PVCs are very common in CHF

• >10 per hour, incidence of NSVT is 90%

• Prior MI → associated with an increased risk of death, especially with LV dysfunction

• NSVT does not add additional risk
Treatment

- Reserved for symptoms or cardiomyopathy
- Beta blockers, CCB
- Antiarrhythmic therapy
- Catheter ablation
### Vaughan Williams classification of antiarrhythmic drugs

<table>
<thead>
<tr>
<th>Class IA - slows conduction velocity (less than class IC) and prolongs action potential duration</th>
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</thead>
<tbody>
<tr>
<td>Disopyramide</td>
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<tr>
<td>Procainamide*</td>
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<td>Quinidine</td>
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<table>
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<tr>
<th>Class IB - has no effect on conduction velocity and may shorten APD</th>
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<tbody>
<tr>
<td>Lidocaine*</td>
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<tr>
<td>Mexiletine</td>
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<td>Phenytin</td>
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<table>
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<tr>
<th>Class IC - slows conduction and may prolong APD (mild)</th>
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<tr>
<td>Flecainide</td>
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<tr>
<td>Propafenone</td>
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<th>Class II - blocks beta adrenergic receptors</th>
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<tr>
<td>Beta blockers</td>
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<tr>
<th>Class III - prolongs APD and has no effect on conduction</th>
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<tbody>
<tr>
<td>Amiodarone</td>
</tr>
<tr>
<td>Dofetilide</td>
</tr>
<tr>
<td>Ibutilide*</td>
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<tr>
<td>Sotalol†</td>
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<tr>
<td>Dronedarone</td>
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<tr>
<th>Class IV - calcium channel blockers</th>
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</thead>
<tbody>
<tr>
<td>Non-dihydropyridine calcium channel blockers (verapamil and diltiazem)</td>
</tr>
</tbody>
</table>

APD: action potential duration.
* Available only as an intravenous preparation in United States. Oral procainamide is available elsewhere.
† I-sotalol has beta blocking and class III activities; d-sotalol is a pure class III agent. Commercially available sotalol is a racemic (equal part) mixture.

**Vaughan Williams EM; Classifying antiarrhythmic actions: by facts or speculation; J Clin Pharmacol 1992; 32:964.**

**Graphic 56600 Version 11.0**
MORTALITY AND MORBIDITY IN PATIENTS RECEIVING ENCAINIDE, FLECAINIDE, OR PLACEBO

The Cardiac Arrhythmia Suppression Trial

Debra S. Echt, M.D., Philip R. Liebson, M.D., L. Brent Mitchell, M.D., Robert W. Peters, M.D., Dulce Obias-Manno, R.N., Allan H. Barker, M.D., Daniel Arensberg, M.D., Andrea Baker, R.N., Lawrence Friedman, M.D., H. Leon Greene, M.D., Melissa L. Huther, David W. Richardson, M.D., and the CAST Investigators*
CAST

- PVCs are associated with an increased risk of sudden and nonsudden cardiac death after MI
- 6 days to 2 years post MI
- EF of less than 55%
- Patients were randomly assigned after establishment of arrhythmia suppression
Results of the Cardiac Arrhythmia Suppression Trial (CAST) in patients with ventricular premature beats after myocardial infarction. Patients receiving encainide or flecainide had, when compared to those receiving placebo, a significantly lower rate of avoiding a cardiac event (death or resuscitated cardiac arrest) (left panel, $p = 0.001$) and a lower overall survival (right panel, $p = 0.0006$). The cause of death was arrhythmia or cardiac arrest.


Graphic 59975 Version 3.0
Effect of amiodarone versus placebo in 1202 postmyocardial infarction patients with ventricular ectopy in the CAMIAT trial. By an intention to treat analysis, amiodarone produced a significant reduction in arrhythmic death (top panel, p = 0.016) but no change in all-cause mortality (bottom panel).

Decreased survival with sotalol in the SWORD trial

Results from the Survival With Oral d-Sotalol (SWORD) trial. The administration of d-sotalol to patients with an ejection fraction ≤40 percent after either recent myocardial infarction (MI) or after symptomatic heart failure with a remote (>42 days) MI was associated with increased mortality compared to placebo (5 versus 3.1 percent). The excess number of deaths was presumed to be primarily due to arrhythmias.

Results of the Beta Blocker Heart Attack Trial which randomized 3837 patients with an acute myocardial infarction to propranolol or placebo. At an average follow-up of 25 months, propranolol significantly reduced total, cardiovascular, and sudden death mortality and reduced the incidence of nonfatal infarction and all coronary events. Benefit occurred in all patient groups, but was more marked in those with heart failure (HF).

Metoprolol reduces mortality in patients with heart failure

The MERIT-HF trial randomly assigned 3991 patients with NYHA class II to IV heart failure who were treated with digoxin, angiotensin converting enzyme inhibitors, and digoxin to metoprolol CR/XL or placebo. Kaplan-Meier curves show a significant reduction in total mortality at 12 months with metoprolol (7.2 versus 11 percent for placebo, p = 0.006).

Catheter Ablation

- ACC/AHA Guidelines
- Frequent, symptomatic, monomorphic PVCs
- > 10,000 PVCs on 24 hour monitor
- Drug resistant, or patient preference
- Ventricular arrhythmia storm initiated by single PVC
Reversal of Cardiomyopathy in Patients With Repetitive Monomorphic Ventricular Ectopy Originating From the Right Ventricular Outflow Tract

Ravi K. Yarlagadda, MD; Sei Iwai, MD; Kenneth M. Stein, MD; Steven M. Markowitz, MD; Bindi K. Shah, MD; Jim W. Cheung, MD; Vivian Tan, MD; Bruce B. Lerman, MD; Sunee Mittal, MD

Background—Tachycardia-induced cardiomyopathy caused by ventricular tachycardia is a well-defined clinical entity. Less well appreciated is whether simple ventricular ectopy can result in cardiomyopathy. We sought to examine a potential causal relationship between repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract and cardiomyopathy and the role of ablation in reversing this process.

Methods and Results—The study consisted of 27 patients (11 men; age, 47±15 years) with repetitive monomorphic ventricular ectopy, including 8 patients (30%) with depressed ventricular function (ejection fraction ≤45%). All patients underwent assessment of cardiac structure and function. The burden of ectopy was quantified through 24-hour Holter monitoring. Patients then underwent ablation guided by 3D mapping. After ablation, patients underwent repeated Holter monitoring and reassessment of cardiac function. Patients with depressed ventricular function were more likely to be older than patients with normal function (58±14 versus 42±18 years; P=0.013). However, the burden of ventricular ectopy was similar in patients with (17 859±13 488 ectopic beats per 24 hours) and without (17 541±11 479 ectopic beats per 24 hours; P=0.800) preserved ventricular function. Successful ablation was performed in 23 patients (85%), including 7 of 8 patients with depressed ventricular function. In this latter group, ventricular function improved in all patients (from 39±6% to 62±6%; P=0.017).

Conclusions—Repetitive monomorphic ventricular ectopy (in the absence of sustained ventricular tachycardia) originating from the right ventricular outflow tract is an underappreciated cause of unexplained cardiomyopathy. Successful ablation of the focal source of ventricular ectopy results in normalization of left ventricular function. Patients with ectopy-induced cardiomyopathy are significantly older than patients with preserved ventricular function, which suggests either that older patients are more susceptible to the development of a cardiomyopathy or that the cardiomyopathy has had a longer period of time in which to evolve. (Circulation. 2005;112:1092-1097.)
Figure 1. Baseline Holter. This continuous 2-minute recording (each of 4 segments represents 30-second period of time) was obtained from patient with repetitive monomorphic ventricular ectopy and depressed left ventricular function (ejection fraction, 30%) who underwent 24-hour Holter monitoring. Frequent monomorphic ectopy is present.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Presenting Symptom</th>
<th>Origin of CMP</th>
<th>Cardiac Medications</th>
<th>PVC Origin in RVOT</th>
<th>RFA Success</th>
<th>Initial Holter, PVCs/24 h</th>
<th>F/U Holter, PVCs/24 h</th>
<th>Initial EF, %</th>
<th>F/U EF, %</th>
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<td>1100</td>
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</tr>
</tbody>
</table>

CMP indicates cardiomyopathy; PVCs, premature ventricular contractions; RFA, radiofrequency ablation; F/U, follow-up; and EF, ejection fraction.

*Patient did not have a 24-hour Holter; however, frequent ambient ectopy was noted on in-patient telemetry.
Conclusion

• Repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract is an underappreciated cause of unexplained cardiomyopathy.

• Successful ablation of the focal source of ventricular ectopy results in normalization of left ventricular function
Case Conclusion
Conclusions

• Most patients have PVCs

• Symptoms, frequency

• Structural heart disease

• PVC cardiomyopathy is typically reversible with catheter radiofrequency ablation
Questions