Ventricular Premature Beats and Heart Failure

Pr Jean-Luc PASQUIÉ
Unité de Rythmologie et Insuffisance cardiaque
INSERM U1046
Département de Cardiologie et Maladies Vasculaires
Hôpital Arnaud de Villeneuve, CHU Montpellier
Déclaration de Relations Professionnelles - Disclosure Statement of Financial Interest

J'ai actuellement, ou j'ai eu au cours des deux dernières années, une affiliation ou des intérêts financiers ou intérêts de tout ordre avec une société commerciale ou je reçois une rémunération ou des redevances ou des octrois de recherche d'une société commerciale :

I currently have, or have had over the last two years, an affiliation or financial interests or interests of any order with a company or I receive compensation or fees or research grants with a commercial company:

**Affiliation/Financial Relationship**

- Grant/Research Support
- Consulting Fees/Honoraria

**Company**

- Medtronic, Boston Sci, Biotronik, Sorin Group, St Jude Medical, Spectranetics, Actelion, Johnson et Johnson
CHF patient survival

Survival, %

Years

No CHF (n=1728)
Class I (n=36)
Class II (n=79)
Class III (n=62)
Class IV (n=59)
Heart Failure and Sudden Death

During a 38-year follow-up of subjects in the Framingham Heart Study, the presence of CHF significantly increased sudden death and overall mortality in both men and women.¹

Severity of Heart Failure

Modes of Death


The greatest opportunity for SCD prevention is in patients that have mild to moderate CHF.
Mortality and Ventricular Arrhythmias in Framingham population

Bikkina M. Annals of Internal Medicine 1992; 117: 990-996
Mechanisms of Death in DCM

Adapted from Bayés de Luna A. Am Heart J. 1989;117:151-159.
VPCs malignancy pattern

“malignant”

• Underlying Heart Disease
• Broad, low voltage
• polyphasic
• polymorphic
• repetitive
• Short coupling, R/T
• number
• + by stress test
• Late potentials
• Inducible VT
PVCs and Cardiomyopathy

• Frequent VPCs 1000 VPCs/24 h :48% of heart failure patients

• PVCs complexity correlates with severity of LV dysfunction

• Patients with decreased LVEF had a higher mean PVC burden than their counterparts with normal LV function
  – 29%–37% versus 8%–13%

• SCDHeFT: NSVT 21-25%
  – Increases when HF worsens: 33.5-36%
  – NSVT associated to lower EF, larger LVEDD, increased furosemide dose, decreased systolic BP, and faster HR

• Frequent VPCs in HF:
  – greater electrical instability of the myocardium
  – marker of arrhythmogenic substrate for increased mortality rate.
VPCs pattern and prognosis

• PVC with broad notching/slurred QRS deflection
  – Diseased myocardial substrate
• PVC > 140 ms
  – Associated to impaired LVEF
VPCs: QRS width as a prognostic criterion

Mean VPC width:
- No Underlying Heart Disease: 140 ms
- Presence of Underlying Heart Disease: 180 ms

Figure 2. Representative tracings of type I (upper panels) and type II (lower panels) premature ventricular complexes. Contrast smooth and uninterrupted contour of narrow type I QRS to notched or shelved, wide type II QRS.

Moulton, Circulation 1990
VT and PVCs Pattern in DCM

Leclercq JF et al. Arch Mal Cœur 1984
Cardiac Mortality in 171 DCM pts

Follow-up 48 ± 42 months, 26 cardiac deaths (12 SD)

Fauchier L et al 2002
Importance on PVC at rest

- 352 patients (64 + or - 11 years; 7 females) with a history of clinical HF
  - 1987-2007, treadmill testing
  - 29.8% had ≥ 1 PVC on the ECG prior to testing
  - Follow-up period of 6.2 years:
- 178 deaths; 42.6% CV causes

- At baseline, patients with at rest PVCs had:
  - a lower EF (30% vs 45%)
  - the prevalence of EF < or = 35% was higher (75% vs 41%)
  - a higher all-cause and CV mortality rate (72% vs 49%, P = 0.01 and 45% vs 20%).
- After adjusting for age, beta-blocker use, rest ECG findings, resting HR, EF, maximal systolic blood pressure, peak HR, and exercise capacity, rest PVC was associated with a 5.5-fold increased risk of CV mortality (P = 0.004).
- Considering the presence of PVCs during exercise and/or recovery did not affect the results.

PVC-induced cardiomyopathy: clinical evidence

- Frequent PVC > 20,000/day or 10%
- PVC > 24%
  - Cut-off impaired/preserved LVEF
  - Specificity 79% sensibility 78%
  - Baman TS et al. *Heart Rhythm*. 2010;7:865–869

- PVC coupling intervals 600 ms: lower mean LVEF

- PVC interpolation: independent predictor of PVC-induced cardiomyopathy
  - Olgun H et al.; *Heart Rhythm*. 2011;8:1046–1049

- Nevertheless, the majority of patients presenting with frequent PVCs has preserved LVEF
PVC-induced cardiomyopathy: clinical evidence

PVC-induced cardiomyopathy: experimental evidence

Left Ventricular Systolic Dysfunction Induced by Ventricular Ectopy A Novel Model for Premature Ventricular Contraction-Induced Cardiomyopathy
Jose F. Huizar, MD et al. Circ Arrhythm Electrophysiol. 2011;4:543-549

- Mongrel dogs n=- vs n= 7 (paced group)
PVC-induced cardiomyopathy: putative mechanisms

- Alterations in intracellular calcium and membrane ionic currents
- Hemodynamic impairment
- Alterations in heart rate dynamics
- Tachycardia-induced cardiomyopathy
- Ventricular dyssynchrony
- Increased oxygen consumption
- Myocardial and peripheral vascular autonomic dysregulation
PVCs and Heart Failure: Is There A Specific Treatment?

• Control Autonomic Imbalance
  – Beta-blockers
  – ACEI

• Improve LV function
  – Beta-blockers
  – ACEI
  – CRT?

• Prevent Arrhythmias
  – Beta-Blockers
  – Amiodarone
  – ICD

Zipes, Wellens Circulation 1998
SCD-HeFT – Total Mortality

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hazard Ratio (97.5% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. placebo</td>
<td>1.05 (0.81–1.36)</td>
<td>0.66</td>
</tr>
<tr>
<td>ICD therapy vs. placebo</td>
<td>0.79 (0.60–1.04)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>426</td>
<td>384</td>
<td>346</td>
<td>227</td>
<td>130</td>
<td>46</td>
</tr>
<tr>
<td>Placebo</td>
<td>453</td>
<td>415</td>
<td>370</td>
<td>244</td>
<td>152</td>
<td>48</td>
</tr>
<tr>
<td>ICD therapy</td>
<td>431</td>
<td>395</td>
<td>365</td>
<td>244</td>
<td>144</td>
<td>48</td>
</tr>
</tbody>
</table>
**Effect of catheter ablation of PVCs on cardiac function**

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Sample Size</th>
<th>Inclusion Criteria</th>
<th>Study Targets</th>
<th>Effect of Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yarlagadda et al. 2005</td>
<td>27 (8 with depressed LVEF &lt;45%)</td>
<td>Frequent PVCs of LBBB and inferior axis morphology (mean of 17 624 PVCs over 24 h on Holter monitoring)</td>
<td>Successful ablation during ablation and remained absent for ≥30 min in baseline state and during infusion of isoproterenol</td>
<td>Successful ablation in 23 patients, including 7 of 8 patients with low LVEF; reduction in PVCs from 17 541 ± 4 479 to 507 ± 722 (P &lt; 0.028)</td>
<td>Significant improvement after ablation in LVEF: mean LVEF increased from 39% ± 6% at baseline to 52% ± 6% (P = 0.017)</td>
</tr>
<tr>
<td>Sekiguchi et al. 2005</td>
<td>47</td>
<td>&lt;10 000 PVCs per d</td>
<td>Reduction in PVCs to &lt;1000 per d</td>
<td>Successful ablation in 38 patients; reduction in PVCs from 23 969 ± 13 366 to 137 ± 249 (P &lt; 0.0001)</td>
<td>After ablation, mean LVDD decreased from 50 ± 5 mm to 48 ± 5 mm (P &lt; 0.01); mean LVESD decreased from 33 ± 7 mm to 30 ± 6 mm (P &lt; 0.01)</td>
</tr>
<tr>
<td>Takemoto et al. 2006</td>
<td>40 (14 with PVC burden &lt;10%; 12, 10%–20%; 14 &gt;20%)</td>
<td>PVCs of LBBB and inferior axis morphology</td>
<td>Successful ablation (noninducibility of PVCs with or without isoproterenol and/or programmed electrical stimulation for ≥30 min, nonrecurrence of PVCs for 72 h)</td>
<td>Successful ablation in 37 patients; reduction in PVC burden in the ≥20% group from 54% ± 3% to 13% ± 0.9% (P &lt; 0.01)</td>
<td>Significant improvement for patients with PVC burden ≥20%; LVDD decreased from 54.1 mm to 47.1 mm, LVEF increased from 66% ± 2% to 72% ± 2%, MR decreased from 1.2 ± 0.2 to 0.3 ± 0.1 and NYHA functional class decreased from 1.8 ± 0.2 to 1.0 ± 0.0 (P &lt; 0.001 for all)</td>
</tr>
<tr>
<td>Bogun et al. 2009</td>
<td>60 or 98</td>
<td>&gt;10 PVCs of LBBB and inferior axis morphology per hour over 24 h on Holter monitoring</td>
<td>Successful ablation</td>
<td>Successful ablation in 48 patients; reduction in PVCs from 17 717 ± 1100 to 260 ± 366 (P = 0.006)</td>
<td>Significant improvement after ablation in LVEF; mean LVEF increased from 59.6 ± 0.6 mm to 51.6 ± 0.6 mm (P = 0.001); LVDD decreased from 54 ± 7 mm to 54 ± 7 mm (P = 0.0002)</td>
</tr>
<tr>
<td>Taieb et al. 2007</td>
<td>6</td>
<td>Frequent PVCs of various morphologies and LV dysfunction (mean of 17 717 PVCs over 24 h on Holter monitoring)</td>
<td>Successful ablation</td>
<td>Successful ablation in all patients; reduction in PVCs from 717 ± 7 to 260 ± 366 (P = 0.006)</td>
<td>Significant improvement after ablation in LVEF; LVEF increased from 42% ± 2.6% at baseline to 57% ± 3% (P = 0.0001), mean LVDD decreased from 60.8 ± 3.5 mm to 54.0 ± 3.7 mm (P = 0.0009)</td>
</tr>
<tr>
<td>Sarrazin et al. 2009</td>
<td>30 (15 referred for ablation, 15 served as control)</td>
<td>PVC burden of &gt;5% in patients with prior myocardial infarction (mean of 17 717 PVCs over 24 h on Holter monitoring)</td>
<td>Successful ablation</td>
<td>Successful ablation in all 15 patients; reduction in PVC burden from 22% ± 12% to 2.6% ± 5.9% (P &lt; 0.001)</td>
<td>Significant improvement after ablation in LVEF; mean LVEF increased from 38% ± 11% to 61% ± 9% (P &lt; 0.0001); no improvement in LVEF was noted in the control group</td>
</tr>
<tr>
<td>Baman et al. 2010</td>
<td>174 (57 with depressed LVEF 35% ± 9%)</td>
<td>Frequent PVCs of various morphologies with normal LVEF, LV volumes, and RV dimensions</td>
<td>Successful ablation (80% reduction in PVC burden)</td>
<td>Successful ablation in 146 patients, including 48 of 57 patients with depressed LVEF; reduction in PVC burden from 33% ± 14% to 1.9% ± 4.4% (P &lt; 0.01)</td>
<td>Significant improvement in the 57 patients with depressed LVEF: LVEF increased from 35% ± 9% at baseline to 54% ± 10% (P &lt; 0.01), LVDD decreased from 59.7 mm to 54.7 mm (P &lt; 0.01), LVESD decreased from 44.7 mm to 39.8 mm (P &lt; 0.01)</td>
</tr>
<tr>
<td>Wijnmaalen et al. 2010</td>
<td>49</td>
<td>PVC burden of &gt;5% of various morphologies with normal LVEF, LV volumes, and RV dimensions</td>
<td>Successful ablation (PVCs abolished during ablation and inducible by isoproterenol)</td>
<td>Successful ablation in 34 patients; reduction in PVC burden from 26% ± 13% to 0.2% ± 0.8% (P &lt; 0.001)</td>
<td>LV radial strain increased from 31.1% ± 4.2% to 46.5% ± 16.3% (P &lt; 0.0001), LV circumferential strain increased from −16.2% ± 3.9% to −18.9% ± 4.2% (P &lt; 0.004), LV longitudinal strain increased from −17.8% ± 2.9% to −19.6% ± 2.6% (P &lt; 0.007), RV longitudinal strain increased from −24.2% ± 7.4% to −26.4% ± 6.0% (P &lt; 0.009)</td>
</tr>
</tbody>
</table>

**Successful ablation is associated with HF improvement**
Effect of catheter ablation of PVCs on cardiac function


51 patients (35 men, 52±15 yo)
  non-ischemic dilated (n=34),
  ischemic (n=12),
  valvular (n=2),
  toxic (2)
  post-partum
29 pts PVC without significant cardiac disease
Daily ventricular premature beats

Left ventricular ejection fraction

**Mean**
- Before RF: 18,000 +/- 9,000
- After RF: 2,800 +/- 4,700

**p < 0.0001**

**Mean**
- Before RF: 41 +/- 10%
- After RF: 52 +/- 13%

**p < 0.0001**

P Maury et al. JE 2013
Arrhythmic Storm and Initiating PVC in DCM

- 48 yo man with DCM, LVEF 15%
- Transplant waiting list
Arrhythmic Storm and Initiating PVC in DCM

• After conventional treatment failure:
  • Life-saving procedure (before heart transplant,..)
Flow chart for the diagnosis, treatment and follow-up of patients presenting frequent premature ventricular contractions

*Circ Arrhythm Electrophysiol. 2012;5:229-236*
CONCLUSIONS

• VPCs in heart failure patients is a difficult problem.
• Problem of sudden death risk stratification in DCM
  – Need for ICD?
• Rule out VPCs-induced CM
• Sometimes RF gives the clue.
Thank You For Your Attention