Dyssynchrony in Ventricular Preexcitation

Eun Jung Bae, M.D.Ph.D.
Department of Pediatrics, College of Medicine,
Seoul National University, Seoul, Korea
• Nothing to disclose
Case. 10Y/female

- 4 years of age: incidentally found cardiomegaly
  → Dx. **Dilated cardiomyopathy with LBBB**
  managed with ACE inhibitor and diuretics
- 6 years of age: visited other H.
  Dx. **WPW syndrome**
- She denied symptoms of palpitation.
- 10 years of age:
  transferred for RF catheter ablation
WPW syndrome
Dilation of left ventricle
Basal IVS: Septal dyskinesia
Thinning of IVS

Biplane Simpson method
EF 20%
early septal flash
Presystolic septal thickening
Before Ao valve opening
Case.

Wall motion abnormality and global dysfunction in WPW syndrome

• Should we ablate the AP without episode of tachycardia?
• Will the wall motion and wall thinning be recovered after RFCA?
• When should we eliminate the AP for complete recovery?
VA dissociation before RFCA

Loss of delta wave during RFCA 2.5sec
RFCA: Paraseptal (anteroseptal) pathway
Improved dyskinesia after RFCA

Before RFCA
AV Preexcitation

2 years after RFCA
No Preexcitation
2 years after RFCA

LVID  53.8/51.5
FS  4.4%
EF  9.9%

Before RFCA

LVID  51.6/39.1
FS  24.1%
EF  47.7%

2 years after RFCA
2D Strain
Pre-excitation related wall motion abnormality and global dysfunction

Mild wall motion abnormality $\rightarrow$ $\rightarrow$ $\rightarrow$ $\rightarrow$ $\rightarrow$ severe LV global dysfunction

Subclinical $\rightarrow$ $\rightarrow$ $\rightarrow$ $\rightarrow$ $\rightarrow$ Clinical

Reversible $\rightarrow$ $\rightarrow$ $\rightarrow$ $\rightarrow$ $\rightarrow$ Irreversible ?

How severe?????
Case Report:

Pre-excitation induced ventricular dysfunction and successful Berlin heart explantation after accessory pathway ablation

20-month-old, WPW: right sided AP (right anterior), severe LV dysfunction
- failed first attempt of RFCA due to hemodynamic instability
- requiring BiVAD (Berlin Heart EXCOR) support, 4 days later listed for cardiac TPL

- 18 days later, the second RFCA: no tachycardia induced, APERP 280ms
  LV dysfunction: completely resolved after successful RFCA of AP, explanted BiVAD
Case Report: Resolution of Dyssynchronous Left Ventricular Failure via Cardiac Resynchronization and Subsequent RFCA in an Infant With Pre-excitation

- 3 months infant with heart failure, d-CMP
  - Transferred for cardiac TPL
  - ECG; WPW syndrome
  → CRT by placing DDD pacemaker
    LV, LA lead via thoracotomy
    100–210/min,
    Very short AV delay (40/70ms)
- 5 years old, RFCA performed for multiple APs
  (right anteroseptal+right lateral)
Dyssynchronous heart by pre-excitation

• Ventricular dilatation
• Asymmetric hypertrophy
• Regional differences
  • in loading and contractile work, wall stress
  • in myocardial blood flow and oxygen consumption
• Regional differences
  • in calcium cycling, in myofilament calcium interactions
  • in matrix fibrosis
  • action potential duration: and freq. early after depolarization

→ Localized myocardial fibrosis

(Circulation. 2003;108:929-932)
Septal Dyskinesia and Global Left Ventricular Dysfunction in Pediatric Wolff-Parkinson-White Syndrome with Septal Accessory Pathway

BO SANG KWON, M.D., EUN JUNG BAE, M.D., GI BEOM KIM, M.D., CHUNG IL NOH, M.D., JUNG YUN CHOI, M.D., and YONG SOO YUN, M.D.

From the Department of Pediatrics, College of Medicine, Seoul National University, Seoul, Korea

LV Dysfunction in WPW Syndrome. Introduction: Echocardiographic studies have shown that some patients with Wolff-Parkinson-White (WPW) syndrome have myocardial dyskinesia in the segments precociously activated by an accessory pathway (AP). The aim of the present study was to determine the extent to which the AP contributes to global left ventricular (LV) dysfunction.

Methods: Electrophysiological and echocardiographic data from 62 children with WPW (age at diagnosis = 5.9 ± 4.2 years) were retrospectively analyzed.

Results: The left ventricular ejection fraction (LVEF) of patients with septal APs (53 ± 11%) was significantly lower than that of patients with right (62 ± 5%) or left (61 ± 4%) APs (P = 0.001). Compared to patients with normal septal motion (n = 56), patients with septal dyskinesia (n = 6) had a reduced LVEF (61 ± 4% and 42 ± 5%, respectively) and an increased LV end diastolic dimension (P < 0.001 for both comparisons). Multivariate analysis identified septal dyskinesia as the only significant risk factor for reduced LVEF. All 6 patients with septal dyskinesia had right septal APs, and a preexcited QRS duration that was longer than that of patients with normal septal motion (140 ± 18 ms and 113 ± 32 ms, respectively; P = 0.045). After RFA there were improvements in both intraventricular dyssynchrony (septal-to-posterior wall motion delay, from 154 ± 91 ms to 33 ± 17 ms) and interventricular septal thinning (from 3.0 ± 0.5 mm to 5.3 ± 2.6 mm), and a significant increase in LVEF (from 42 ± 5% to 67 ± 8%; P = 0.001).

Conclusion: The dyskinetic segment activated by a right septal AP in WPW syndrome may lead to ventricular dilation and dysfunction. RFA produced mechanical resynchronization, reverse remodeling, and improvements in LV function. (J Cardiovasc Electrophysiol, Vol. 21, pp. 290-295, March 2010)
62 children with WPW syndrome, RFCA

Global LV function and location of AP

All recovered after RFCA

Global LV dysfunction, EF < 50%
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at diagnosis/ RFA (yr)</th>
<th>F/U after RFA (yr)</th>
<th>LVIDd$^+$ (pre/post-RFA) (Z-score)</th>
<th>EF$^\prime$ (pre/post-RFA / Latest f/u) (%)</th>
<th>SPWMD$^\dagger$ (pre/post-RFA) (ms)</th>
<th>Sphericity index (pre-RFA) (ED$^\parallel$/ES$^\parallel$)</th>
<th>Sphericity index (post-RFA) (ED$^\parallel$/ES$^\parallel$)</th>
<th>Basal IVS$^#$ (pre/post-RFA) (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.8 / 8.2</td>
<td>0.1</td>
<td>+1.69/ +0.89</td>
<td>37 / 45 / -</td>
<td>170 / -</td>
<td>0.66/0.79</td>
<td>0.79/0.71</td>
<td>2.9 / 3.2</td>
</tr>
<tr>
<td>2</td>
<td>7.4 / 13.7</td>
<td>7.4</td>
<td>+1.36 / +0.53</td>
<td>39 / 53 / 59</td>
<td>- / 90</td>
<td>-/ -</td>
<td>0.68/0.86</td>
<td>3.2 / 4.8</td>
</tr>
<tr>
<td>3</td>
<td>0.1 /4.9</td>
<td>1.5</td>
<td>+1.54 / +0.41</td>
<td>39 / 52 / 59</td>
<td>100 / 60</td>
<td>0.88/0.79</td>
<td>0.87/0.85</td>
<td>2.8 / 5.4</td>
</tr>
<tr>
<td>4</td>
<td>6.0 / 8.7</td>
<td>2.0</td>
<td>+2.59 / +2.42</td>
<td>41 / 63 / 70</td>
<td>140 /46</td>
<td>0.81/0.89</td>
<td>0.71/0.73</td>
<td>2.8 / 4.2</td>
</tr>
<tr>
<td>5</td>
<td>0.4 /8.1</td>
<td>6.5</td>
<td>+0.89 / +0.60</td>
<td>43 / 55 / 77</td>
<td>299 / 14</td>
<td>-/-</td>
<td>0.65/0.49</td>
<td>2.3 / 5.4</td>
</tr>
<tr>
<td>6</td>
<td>6.3 / 8.0</td>
<td>0.8</td>
<td>+1.58 / +0.67</td>
<td>50 / 64 / 70</td>
<td>60 / 39</td>
<td>0.85/0.78</td>
<td>0.81/0.57</td>
<td>3.7 / 3.9</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>4.2±3.1/ 8.6±2.8</td>
<td>3.1±3.1</td>
<td>+1.61±0.56/ +1.03±0.80</td>
<td>42±5 / 55±7 / 67±8</td>
<td>154 ± 91 / 33 ± 17</td>
<td>0.80 ± 0.10 / 0.81 ± 0.05</td>
<td>0.75 ± 0.08/ 0.70 ± 0.15</td>
<td>3.0 ± 0.5 / 5.3 ± 2.6</td>
</tr>
</tbody>
</table>
Location of AP
WPW and LV dysfunction

<table>
<thead>
<tr>
<th></th>
<th>year</th>
<th>N</th>
<th>median age</th>
<th>location</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kwon, Bae et al</td>
<td>2010</td>
<td>15</td>
<td>4.2/8.6 RFCA</td>
<td>Septal (n=14) Inferoparaseptal (n=1)</td>
<td>all, 6m</td>
</tr>
<tr>
<td>Udink ten Cate et al</td>
<td>2010</td>
<td>8</td>
<td>8 (1-17)</td>
<td>Supero-paraseptal/septal (n=7) Fasciculoventricular P(n=1)</td>
<td>all, 1.5m</td>
</tr>
<tr>
<td>Tomaske et al</td>
<td>2008</td>
<td>19</td>
<td>14</td>
<td>Paraseptal n=13 septal n=6</td>
<td>all</td>
</tr>
<tr>
<td>Emmel et al</td>
<td>2004</td>
<td>4</td>
<td>8 (1-12)</td>
<td>Right n=4</td>
<td>all</td>
</tr>
<tr>
<td>CC Dai et al</td>
<td>2013</td>
<td>4</td>
<td>8</td>
<td>Right n=2, Supero-septal n=2</td>
<td>all</td>
</tr>
<tr>
<td>Uhm et al</td>
<td>2018</td>
<td>30</td>
<td>37.6 (adult)</td>
<td>Dyskinesia, Rt n=13, Septal n=15 left n=2</td>
<td>20/30</td>
</tr>
</tbody>
</table>
Altered myocardial characteristics of the preexcited segment in Wolff-Parkinson-White syndrome: A pilot study with cardiac magnetic resonance imaging

- Prospective study, 22 adult WPW syndrome pts (16 male, mean 45.4 ± 17.8 years) with echocardiographic findings of regional wall motion abnormality

- The late gadolinium enhancement (LGE) (9/22, 40.9%): exclusively at the basal septum.

- The septal accessory pathway: more prevalent in patients with LGE ($P = 0.011$).

- LGE
  - regional myocardial wall thinning
  - regional akinesia ($P = 0.001$ for both)
  - left ventricular dysfunction ($P < 0.001$)
67-year-old female patient with WPW syndrome: posteroseptal AP. LV EF 47%
Comparison of CMR findings according to the presence of LGE.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 22)</th>
<th>LGE (-) (n = 13)</th>
<th>LGE (+) (n = 9)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AP location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>4 (18.2%)</td>
<td>3 (23.1%)</td>
<td>1 (11.1%)</td>
<td>0.616</td>
</tr>
<tr>
<td>Septal</td>
<td>14 (63.6%)</td>
<td>6 (46.2%)</td>
<td>8 (88.9%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Left</td>
<td>4 (18.2%)</td>
<td>4 (30.8%)</td>
<td>0 (0.0%)</td>
<td>0.046</td>
</tr>
<tr>
<td><strong>Wall thinning</strong></td>
<td>6 (27.3%)</td>
<td>0 (0.0%)</td>
<td>6 (66.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>RWMA</strong></td>
<td>13 (5.1%)</td>
<td>4 (30.8%)</td>
<td>9 (100.0%)</td>
<td>0.002</td>
</tr>
<tr>
<td>remature contraction</td>
<td>7 (31.8%)</td>
<td>4 (30.8%)</td>
<td>3 (33.3%)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td><strong>Akinesia</strong></td>
<td>6 (27.3%)</td>
<td>0 (0.0%)</td>
<td>6 (66.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td>LVEDV (ml/BSA)</td>
<td>90.8 ± 30.9</td>
<td>76.0 ± 8.3</td>
<td>112.4 ± 38.9</td>
<td>0.003</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>56.7 ± 12.0</td>
<td>64.1 ± 5.0</td>
<td>45.9 ± 10.8</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
The effect of RFCA in adult WPW syndrome with regional wall motion abnormality

Median time interval from RFA to CMR:
465.5 (IQR, 276.5±709.5) days for the 14 patients with RFA.

| Table 3. Comparison of major findings according to performance of RFA. |
|---------------------------------|-----------------|-----------------|--------|
|                                 | RFA (+) (n = 14)| RFA (-) (n = 8) | P value |
| RWMA                            | 5 (35.7%)       | 8 (100.0%)      | 0.006  |
| Premature contraction           | 1 (7.1%)        | 6 (75.0%)       | 0.002  |
| Akinesia                        | 4 (28.6%)       | 2 (25.0%)       | > 0.999|
| Wall thinning                   | 4 (28.6%)       | 2 (25.0%)       | > 0.999|
| LGE                             | 5 (35.7%)       | 4 (50.0%)       | > 0.999|
| Low ejection fraction           | 4 (28.6%)       | 3 (37.5%)       | > 0.999|

Myocardial fibrosis in the preexcited myocardium of adult WPW syndrome -may cause persistent left ventricular systolic dysfunction even after radiofrequency ablation.
Dyssynchronous Heart

WPW syndrome
Atrioventricular preexcitation

Dysbalance in gene expressions btw Early and late activated regions

Dyskinesia
Septal thinning
Akinesia
Irreversible change with LGE

Fibrosis with aging

Fibrosis with aging
Summary

• A group of WPW syndrome patients may have coexisting DCM, with dyskinesia/akinesia or regional wall motion abnormalities.
• The location of AP: usually right sided, paraseptal/septal
• RFCA may cause reverse remodeling and recovery of LV function.
• Long standing dyskinesia/akinesia may not recovered after RFCA, especially in adult age.
• AP with dyskinesia/akinesia: should be eliminated by RFCA regardless of tachycardia.
Set diagram for the logical relations between the major findings
Dyssynchronous Heart Failure

Molecular Portrait

Regional Changes

Dysbalance in Gene Expression between Late and Early-activated Regions

- Ca\textsuperscript{2+}-handling proteins
  - SERCA \downarrow
  - PLN \downarrow
  - SERCA / PLN \downarrow
- ECM matrix remodelling
- stress response
- Electrical remodelling
- Foetal gene Program \uparrow

Global Changes

- Mitochondrial Proteome
  - Δ-Pyruvate metabolism
  - Δ-Krebs cycle
  - Δ-Respiratory Chain Subunits
  - Complex V \uparrow
- Apoptosis
  - Apoptotic index \uparrow
- Beta-adrenergic system
  - β1-receptors \downarrow
  - RGS proteins \downarrow

References:
Circulation. 2003;108:929-932
Regional Myocardial Abnormalities in Patients With WPW Syndrome With the Use of ECG-Gated Cardiac MDCT