Remodeling and Recovery in Peripartum Cardiomyopathy:

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18 year old woman two weeks post partum:
LVEF 18% with marked biventricular enlargement
Remodeling in PPCM

- LVEF at presentation predicts outcomes
- Remodeling (LV end diastolic diameter or LVEDD) is potentially a stronger predictor of recovery
- Factors which impact recovery do so through an impact on remodeling
Physiologic Left Ventricular Remodeling in Pregnancy

- Important adaptation to sustained “volume work”
- Increased SV to increase CO and provide for placental blood flow
- Rapid reverse remodeling in the early post partum phase

Savu et al, Circ Cardiovasc Imaging, 2012
### Variables

#### Dimensions

<table>
<thead>
<tr>
<th>Variables</th>
<th>A) Female controls</th>
<th>B) Second trimester</th>
<th>C) Third trimester</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventricular septum (cm)</td>
<td>0.77±0.12&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.81±0.10</td>
<td>0.84±0.11&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.045</td>
</tr>
<tr>
<td>Posterior wall thickness (cm)</td>
<td>0.75±0.14&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.82±0.10</td>
<td>0.86±0.10&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.002</td>
</tr>
<tr>
<td>LV Dimension, diastole (cm)</td>
<td>4.5±0.3</td>
<td>4.8±0.4</td>
<td>4.7±0.4</td>
<td>0.05</td>
</tr>
<tr>
<td>LV Dimension, systole (cm)</td>
<td>2.8±0.3&lt;sup&gt;bbb,c&lt;/sup&gt;</td>
<td>3.2±0.3&lt;sup&gt;aaa&lt;/sup&gt;</td>
<td>3.0±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV Mass index (g/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>63±12&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>71±9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>72±14&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.018</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.34±0.07</td>
<td>0.35±0.07</td>
<td>0.37±0.05</td>
<td>0.145</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62±3</td>
<td>62±4</td>
<td>63±4</td>
<td>0.302</td>
</tr>
</tbody>
</table>

#### Volumes

| LA Volume (ml)                          | 36±7<sup>bb,c</sup> | 44±14<sup>aa</sup> | 44±13<sup>a</sup> | 0.006   |

LV: Left ventricular, DT: deceleration time, LVEF: Left ventricle ejection fraction, LA: Left atrium, RVSP: Right ventricular systolic pressure, LAVI: Left atrium volume index.

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Proportional Increase in Hypertrophy and LVEDD

Ando et al, AmJ Card 2015
Investigation of Pregnancy Associated Cardiomyopathy: (IPAC)

- Prospective investigation, 100 women newly diagnosed with PPCM
- Clinical, biomarker and genetics predictors of recovery
- Network of 30 centers
  http://www.peripartumcmnetwork.pitt.edu
LVEF <0.30 and Recovery in IPAC

JACC, 2015
LVEDD $\geq 6.0$ cm and Recovery in PPCM

JACC, 2015
Clinical Predictors, Remodeling and Recovery

- BMI
- Race
- Diabetes
BMI and recovery in PPCM

- $p=0.02$ at 6 month,
- $P=0.015$ at 12 months

Davis, AHA 2015
LVEF over time: normal or underweight (BMI<25), overweight (25 to 29.9), obese (BMI≥30)

Davis, AHA, 2015
LVEDD by BMI

- BMI $\leq 25$
- 25 to 30
- BMI $\geq 30$

Total: $P < 0.001$
White: $P < 0.001$
Black: $P = 0.03$

Davis, AHA 2015
Myocardial Recovery by race in IPAC:
LVEDD by Race: BMI subsets (IPAC)

- **Overall BMI >=30**
  - Black: 5.8 ± 0.07 (N=29)
  - White/Other: 5.5 ± 0.06 (N=70)
  - p=0.03

- **BMI >30**
  - Black: 6.1 ± 0.07 (N=13)
  - White/Other: 5.8 ± 0.07 (N=24)
  - p=ns

- **BMI <30**
  - Black: 5.6 ± 0.05 (N=16)
  - White/Other: 5.3 ± 0.06 (N=46)
  - p=ns

**Davis, AHA 2015**
LVEF Recovery by Diabetes (IPAC)

Baseline
- Diabetes: 34 (±11), N=11
- No Diabetes: 34 (±9), N=89
  - p=0.90
  - N=100

6 month
- Diabetes: 44 (±12), N=9
- No Diabetes: 52 (±10), N=70
  - p=0.02
  - N=79

12 month
- Diabetes: 49 (±11), N=10
- No Diabetes: 54 (±10), N=66
  - p=0.16
  - N=76

Abraham, ACC 2018
LVEDD by Diabetes: BMI subsets (IPAC)

Overall BMI >=30 BMI <30

Diabetes No Diabetes

LVEDD (cm)

Overall

BMI >=30

BMI <30

N=99

N=37

N=62

p=0.04

p=ns

p=ns

Abraham, ACC 2018
Diabetes, BMI, Race and Recovery

Diabetes → BMI → Race → LVEDD → LV Recovery
Diabetes, BMI, Race and Recovery

Diabetes  BMI  Race

Vascular changes, myocyte apoptosis, inflammation, fibrosis

LVEDD

LV Recovery
Leptin:

• 16 KD hormone secreted by adipose tissue

• Promotes vascular inflammation, oxidative stress and vascular smooth cell proliferation.

• Levels increase in HF subjects
Relationship of Leptin/BMI

- Overall: p<0.00001, Constant -26409.67, B1=1803
- Black: p=0.000001, Constant -47927.46, B1=2652
- Non-Black: p=0.000001, Constant -15989.013, B1=1354

Davis AHA, 2015
Leptin by Race and Diabetes

Diabetic (vs non)
- 21,856
- 38,534

Black (vs white/other)
- 20,878
- 30,747

p = 0.01

Davis, AHA 2015
LVEDD and LVESD
IPAC subjects by Leptin tertiles

\[
\begin{array}{c|c|c|c}
\text{Leptin tertiles} & \text{LVEDd} & \text{LVEDs} \\
\hline
\text{low} & 5.5 & 5.5 \\
\text{med} & 5.9 & 4.4 \\
\text{high} & 4.9 & 4.6 \\
\end{array}
\]

\[p=0.008\]
\[p=0.015\]

Davis, AHA, 2015
Diabetes, BMI, Race and Recovery

Diabetes → BMI → Race → Leptin

向上箭头表示增加：LVEDD
向下箭头表示减少：LV Recovery
Diabetes, BMI, Race and Recovery

Diabetes → BMI → Race → Leptin

Leptin → titin, sFlt1, 16Kd prolactin

Leptin → LVEDD

LVEDD → LV Recovery
Remodeling in Peripartum Cardiomyopathy

• For women presenting with PPCM, the degree of remodeling (LVEDD) appears to predict potential recovery

• Race, BMI, Diabetes, all impact the degree of remodeling

• Interventions which prevent or limit remodeling should facilitate recovery
Peripartum Cardiomyopathy Network (PCN)

- http://www.peripartumcmnetwork.pitt.edu
- mcnamaradm@upmc.edu