BMI, Ventricular Remodeling, and Recovery in PPCM

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No disclosures necessary
Obesity, Metabolic Syndrome and the Maternal CV outcomes

- **Metabolic syndrome, diabetes increase CV risk**

- **Increasingly investigated in maternal PP outcomes**

- A “Cardiomyopathy of Obesity” postulated but does it indeed exist?
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
Hypothesis (Dr. Davis):

- Adverse Association of Maternal BMI with Recovery in PPCM
- Biomarkers associated with increase BMI (leptin) would adversely impact recovery
- Does BMI or associated biomarkers influence racial differences in outcomes?
Method:

• Compared by BMI at entry: Obese (BMI>30), Overweight (25-30) and normal/underweight (<25)

• Biomarkers: correlation with BMI, mean levels in recovered vs not, and changes in LVEF by tertiles

• Relationship of BMI, Leptin, LVEDD compared by multivariate and mediation analysis
### IPAC Cohort (n=100)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>$30 \pm 6$ (18-43)</td>
</tr>
<tr>
<td>Gravida</td>
<td>$2.8 \pm 1.9$ (1-10)</td>
</tr>
<tr>
<td>Para</td>
<td>$2.2 \pm 1.4$ (1-6)</td>
</tr>
<tr>
<td>Race (W / B / A / Other)</td>
<td>65 / 30 / 1 / 4</td>
</tr>
<tr>
<td>NYHA Class (1-4)</td>
<td>12 / 47 / 24 / 17</td>
</tr>
<tr>
<td>BP (sys)</td>
<td>$112 \pm 17$</td>
</tr>
<tr>
<td>BP (dia)</td>
<td>$70 \pm 13$</td>
</tr>
<tr>
<td>beta blockers (entry)</td>
<td>88%</td>
</tr>
<tr>
<td>ACEI/ARB (entry)</td>
<td>81%</td>
</tr>
<tr>
<td>Days post partum</td>
<td>$31 \pm 24$ (0-91)</td>
</tr>
</tbody>
</table>
LVEF over time: normal or under (BMI<25), overweight (25 to 29.9), obese (BMI≥30)

* p=0.40
* p=0.001
* p=0.01
* p=0.03

Davis, AHA, 2015
### Biomarkers: Metabolic

**Leptin: strong correlation with BMI**

<table>
<thead>
<tr>
<th></th>
<th>Pearson</th>
<th>Spearman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin</td>
<td>r 0.484</td>
<td>0.558</td>
</tr>
<tr>
<td></td>
<td>p 0.000001</td>
<td>0.0000001</td>
</tr>
<tr>
<td>adiponectin</td>
<td>r -0.159</td>
<td>-0.201</td>
</tr>
<tr>
<td></td>
<td>p 0.123</td>
<td>0.051</td>
</tr>
<tr>
<td>oxLDL</td>
<td>r 0.174</td>
<td>0.110</td>
</tr>
<tr>
<td></td>
<td>p 0.092</td>
<td>0.287</td>
</tr>
<tr>
<td>sFAS</td>
<td>r 0.215</td>
<td>0.175</td>
</tr>
<tr>
<td></td>
<td>p 0.036</td>
<td>0.090</td>
</tr>
<tr>
<td>TNF</td>
<td>r 0.173</td>
<td>0.788</td>
</tr>
<tr>
<td></td>
<td>p 0.093</td>
<td>0.053</td>
</tr>
</tbody>
</table>
Leptin:

- 16 KD hormone secreted by adipose tissue
- Promotes vascular inflammation, oxidative stress and vascular smooth cell proliferation.
- Levels increase in HF subjects
Leptin by Race, Diabetes, and Multiple Birth

- **Diabetes**: 21,856 (±19,790) vs. 20,878 (±20,515)  
  - *p*=0.01

- **Black race**: 38,534 (±27,542) vs. 30,747 (±22,045)  
  - *p*=0.04

- **Multiple birth**: 26,323 (±22,045) vs. 13,644 (±22,045)  
  - *p*=0.02
Leptin (ng/ml) significantly lower in subjects who recovered (final LVEF $\geq 0.50$)

<table>
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<tr>
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<th>No Recovery</th>
<th>Recovered</th>
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<tr>
<td>Leptin (ng/ml)</td>
<td>33 ± 23</td>
<td>20 ± 19</td>
</tr>
</tbody>
</table>

$n=31$ for no recovery, $n=64$ for recovered

$p=0.005$

Davis, AHA, 2015
LVEDD and LVESD for all patients by Leptin Tertiles

- LVEDd: 5.5, 5.5, 5.9
- LVESd: 4.4, 4.6, 4.9

p=0.008 for LVEDd
p=0.015 for LVESd

Davis, AHA, 2015
Recovery of LVEF by Leptin level (overall tertiles)

- **baseline**: Low (000 - 9500) = 0.35 ± 0.09, Mid (9501 - 26000) = 0.42 ± 0.12, High (>26000) = 0.41 ± 0.11
- **2 month**: Low = 0.53 ± 0.10, Mid = 0.53 ± 0.12, High = 0.49 ± 0.11
- **6 month**: Low = 0.57 ± 0.08, Mid = 0.52 ± 0.09, High = 0.51 ± 0.10
- **12 mon**: Low = 0.56 ± 0.08, Mid = 0.53 ± 0.09, High = 0.51 ± 0.08
- **last EF**: Low = 0.56 ± 0.09, Mid = 0.53 ± 0.09, High = 0.51 ± 0.09

Significance levels:
- p=0.97 (baseline)
- p=0.04 (2 month)
- p=0.19 (6 month)
- p=0.048 (12 mon)
- p=0.04 (last EF)
LVEDD by BMI and Race

Mean LVEDD (cm)

- Total: P<0.001
- White: P<0.001
- Black: P=0.03
Relationship: BMI/LVEDD

Overall: $p=0.00002$, Constant=46.262, $B1=0.350$

Black: $p=0.024$
Constant=46.630, $B1=-0.384$

Non-Black: $p=0.001$
Constant=46.694, $B1=0.313$
Relationship of BMI, LVEDD, Leptin and Recovery

BMI

LVEDD

LVEF 12 mo
Relationship of Leptin/BMI

Overall: $p < 0.000001$, Constant -26409.67, $B_1 = 1803$

Black: $p = 0.000001$
Constant -47927.46
$B_1 = 2652$

Non-Black: $p = 0.000001$
Constant -15989.013
$B_1 = 1354$
Relationship of BMI, LVEDD, Leptin and Recovery

BMI → LVEDD → LVEF 12 mo
Relationship of BMI, LVEDD, Leptin and Recovery

BMI → Leptin

LVEDD → ?

LVEF 12 mo → LVEDD
BMI, LVEDD, and recovery in PPCM

- In IPAC, a higher BMI at entry was associated with a lower 12 month LVEF.

- This is the first study to indicate a role for obesity in the formation of non-ischemic cardiomyopathy.

- BMI was tightly correlated with LVEDD, and the impact of BMI is primarily mediated though an impact on LV remodeling.
Leptin, BMI and remodeling

- Leptin levels are tightly correlated with BMI.
- Leptin levels are higher in Blacks and higher in subjects who do not recover.
- Role as a mediator of ventricular remodeling less certain.
Peripartum Cardiomyopathy Network (PCN)

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