A decade of hemodynamic surveillance in Appalachian pregnancies

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Joan C. Edwards School of Medicine
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Disclosures
• I owned 10% of a software patent for the database I use to manage hemodynamics
  – No more software patents!
• With another investor I now own 50% of the restructured remaining debt of the company we started
A fundamental premise of treatment studies is that all patients in the study have the same disease...
Clinical Scenario

• 24yo G1P0 at 24 weeks presents to OB triage with complaints of shortness of breath and a respiratory rate of 26.
Clinical Scenario

• 24yo G1P0 at 24 weeks presents to OB triage with complaints of shortness of breath and a respiratory rate of 26.
  – What medication would you start:
    • Low molecular weight heparin
    • Nebulized beta agonists
    • Intravenous antibiotics
What? You want more information?

• 10% untreated mortality
What? You want more information?

Randomized trial in treatment of SOB in 300 patients

<table>
<thead>
<tr>
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<th>Mortality</th>
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<tbody>
<tr>
<td>Lovenox</td>
<td>6.7%</td>
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<tr>
<td>Inhaled beta agonists</td>
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<td>6.7%</td>
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<td>Lovenox</td>
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<td>0</td>
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Sutton’s Law
Beginnings
How does cardiac output vary with gestational age?

How does cardiac output vary with gestational age?

## Preeclamptic Hemodynamics

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<tr>
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Clinical Use
Randomized Trial

### Clinical Use (n=250)

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<th>Condition</th>
<th>Expected</th>
<th>Observed</th>
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<td>Severe preeclampsia</td>
<td>18%</td>
<td>1 (0.4%)</td>
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<tr>
<td>Delivery &lt; 34 wks</td>
<td>30%</td>
<td>11 (4.7%)</td>
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<td>30%</td>
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</tr>
<tr>
<td>Birthweight</td>
<td></td>
<td>2828</td>
</tr>
<tr>
<td>&lt;10th %tile</td>
<td></td>
<td>20%</td>
</tr>
<tr>
<td>Fetal Demise</td>
<td></td>
<td>1(0.4%)</td>
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BioZ
Impedance Cardiography Standards

NICaS
Non Invasive Cardiac System
NICas vs Thermodilution

\[ r = 0.90; \quad \text{Bias} = -0.114; \quad \text{Precision} = 0.982 \]

NI Medical Meets FDA requirements for claiming Statistical Bioequivalence to Thermodilution CO (1)

The Population

- Examined 2738 patients Jan 2005 – Dec 2014
  - CHTN, DM, Prior preterm preeclampsia, chronic renal disease
  - Monitoring beta blockade for other indications
  - Multiple delivering hospitals
- Data on 2265 infants delivered at Cabell
- After excluding miscarriages, twins, preconception exams and initial exams after 24 weeks – 1864 pregnancies
The Protocol

• Monthly hemodynamic evaluation
  – Starting as early as possible for elevated BP or on medications
  – Start 16-24 weeks for history
  – Monthly growth sonograms
  – At 32 weeks start 2x/week fetal testing
  – Deliver by 39 weeks
The Protocol

• Monthly hemodynamic evaluation
• Treat hyperdynamic state (CO > 7.4 and SVR < 1100) with beta blockers
  – Atenolol, metoprolol, propranolol
The Protocol

• Monthly hemodynamic evaluation
• Treat hyperdynamics with beta blockers
• Treat vasoconstricted
  – Need rate control and vasodilation
    • Beta blocker + nifedipine XL or amlodipine
    • Nebivolol (beta + NO), carvedilol (beta + $\alpha_1$block)
    • Clonidine
The Protocol

- Monthly hemodynamic evaluation
- Treat hyperdynamics with beta blockers
- Treat vasoconstricted
- Half of this cohort (896) was treated with atenolol
Hemodynamics at first exam

MAP mmHg vs Cardiac Output Lpm

- Hyperdynamic
- Normal
- Vasoconstricted
Hemodynamics at first exam
Some patients remained normal
Obesity

[Graph showing relationship between MAP mmHg and Cardiac Output with data points and a line indicating BMI < 30, 31%]
Obesity

![Graph showing the relationship between Cardiac Output and MAP mmHg. The x-axis represents Cardiac Output with values from 2 to 16, and the y-axis represents MAP mmHg with values from 60 to 160. The graph includes a line indicating BMI 31-40, which affects 42% of the population.]
Obesity
Hypertension Subsets

MAP mmHg vs Cardiac Output LPM

BP<140/90
Hypertension Subsets

MAP mmHg vs Cardiac Output LPM

- BP<140/90
- BP 140-149/90-99
Hypertension Subsets

- BP<140/90
- BP 140-149/90-99
- BP 150-159/100-109
Hypertension Subsets

MAP mmHg vs Cardiac Output LPM

- BP<140/90
- BP 140-149/90-99
- BP 150-159/100-109
- BP>160/110
Chronic Hypertension

The graph shows a scatter plot with data points indicating cardiac output (Lpm) on the x-axis and mean arterial pressure (MAP mmHg) on the y-axis. The data points cluster around the line marking chronic hypertension, which is typically defined by an elevated MAP.
Diabetes
Outcomes

- Perinatal Mortality
- SGA
- Preterm Birth
- Preeclampsia
Outcomes

- Perinatal Mortality
  - FDU (1.2%, half < 24 weeks)
  - Neonatal Death (1.1%, 40% < 24 weeks)
- SGA
- Preterm Birth
- Preeclampsia
Perinatal Outcomes

Frequencies

<table>
<thead>
<tr>
<th>Level</th>
<th>Count</th>
<th>Prob</th>
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<tbody>
<tr>
<td>FDU</td>
<td>22</td>
<td>0.01180</td>
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<tr>
<td>NICU</td>
<td>250</td>
<td>0.13412</td>
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<tr>
<td>Neonatal Death</td>
<td>21</td>
<td>0.01127</td>
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<tr>
<td>Normal Nursery</td>
<td>1571</td>
<td>0.84281</td>
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<tr>
<td>Total</td>
<td>1864</td>
<td>1.00000</td>
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Stillbirths
Perinatal Mortality
SGA

MAP mmHg vs Cardiac Output LPM scatter plot.
Preterm Delivery

![Graph showing correlation between MAP mmHg and Cardiac Output LPM. Points are scattered across the graph with a trend line indicating increased Cardiac Output with higher MAP values.]
Chronic Hypertension
### Frequencies

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<tr>
<td>NICU</td>
<td>144</td>
<td>0.14984</td>
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<tr>
<td>Neonatal Death</td>
<td>11</td>
<td>0.01145</td>
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<tr>
<td>Normal Nursery</td>
<td>795</td>
<td>0.82726</td>
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<tr>
<td>Total</td>
<td>961</td>
<td>1.00000</td>
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</table>
Gestational Age at Delivery
Preterm Delivery %

- BP <140/90
- BP 140-149/90-99
- BP 150-159/100-109

Delivery < 35 weeks

SGA %

![Bar chart showing SGA % for different blood pressure ranges (BP < 140/90, BP 140-149/90-99, BP 150-159/100-109). The chart compares Marshall and MFMU* results.](image)

Perinatal Mortality %

Comparison to Two Recent Studies

Comparison to Two Recent Studies

### Table 2 Maternal and Fetal Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hyperdynamic ($n = 242$)</th>
<th>Mixed Hemodynamics ($n = 76$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wk)</td>
<td>36.8 ± 2.1</td>
<td>35.6 ± 2.6</td>
</tr>
<tr>
<td>Birth weight percentile</td>
<td>51.8 ± 27</td>
<td>43.6 ± 26</td>
</tr>
<tr>
<td>Preeclampsia (all)</td>
<td>24 (10%)</td>
<td>20 (27%)</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>6 (2.5%)</td>
<td>7 (9.2%)</td>
</tr>
</tbody>
</table>
Comparison to Two Recent Studies

Summary

• Now we have a choice
  – Choose your favorite drug
  OR
  – “Less tight” vs “More tight” control
  OR
  – Treatment guided by hemodynamics

• Advantages of knowledge
  – Decreased perinatal mortality
  – Decreased growth restriction
  – Decreased preeclampsia