Treatment of Decompensated Left-sided Heart Failure Lowers Right Ventricular Pulsatile Load and Increases the Pulmonary Arterial Time Constant

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Disclosures

• None
Background

*In left-sided heart failure*

- Right ventricular (RV) dysfunction determines:
  - Poor prognosis
  - Exercise intolerance

- Reasons for RV dysfunction:
  - Similar cardiomyopathic process
  - Decreased coronary perfusion
  - Ventricular interdependence
  - Septal dysfunction
  - Increased afterload due to failing left ventricle
Background

*How to quantify afterload?*

- 3-element Windkessel model
  - Peripheral resistance $R$
    - Small vasculature
  - Characteristic impedance $Z$
    - Proximal vessel
  - Arterial compliance $C$
    - Whole vasculature
Background

In clinical practice

- Pulmonary Vascular Resistance (PVR)

\[
\text{mean PA - PCWP} \\
\text{CO}
\]

- Pulmonary Arterial Capacitance (PAC)

\[
\text{Stroke Volume} \\
\text{Pulse Pressure}
\]
Background

*In Pulmonary Arterial Hypertension*

1. \[ \text{PVR} \times \text{PAC} = \tau = \text{Cte} \]

2. PAC has higher prognostic significance

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Study Aims

*In left-sided heart failure*

1. To examine the relationship between PVR and PAC

2. To compare PVR with PAC as predictor of
   1. RV failure
   2. Prognosis

3. To examine the change in PVR and PAC after successful decongestion
Methods

Aim 1 and 2: Relationship with PVR & Prognosis of PAC

- 724 patients (2000 – 2005) referred for RHC
- Primary outcome: Death + HTX

Aim 3: Influence of Treatment

- 75 patients (2010-2011) admitted for hemodynamically tailored therapy for ADHF
- Successful decongestion defined as drop in PCWP > 10 mmHg
Methods

• Single center retrospective study
• Echocardiographic data (30 days before RHC)
  – Visual assessment RV function (grade 0 - 4)
  – RV failure = grade 3 or 4 hypokinetic motion
Results

PVR and PAC

Pulm Capac = 0.35/PVR
Results

**PVR and PAC as a function of PCWP**

Wedge ≤ 17: Pulm Capac = 0.43/PVR
Wedge > 17: Pulm Capac = 0.30/PVR
P < 0.01
Results

$\tau$ as function of PCWP

$r = -0.42$

$\tau = 0.52 - 0.0085 \times \text{wedge pressure}$
Results

Afterload parameters and RV failure

ROC curve

P = 0.003

PAC AUC = 0.74
Wedge AUC = 0.71
PVR AUC = 0.67
Results

Survival as function of afterload parameters

A. PAC Quartiles

B. PVR Quartiles

Days to death or transplant

Free from death or transplant

PAC < 1.60
1.60 ≤ PAC < 2.50
2.50 ≤ PAC < 3.95
PAC ≥ 3.95

PVR ≥ 3.23
2.11 ≤ PVR < 3.23
1.40 ≤ PVR < 2.11
PVR < 1.40
# Results

## Cox-model predicting death/HTX

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Hazard ratio per 1 increment death or transplant</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA</td>
<td>1.09 (0.85-1.40)</td>
<td>0.50</td>
</tr>
<tr>
<td>Age</td>
<td>1.00 (0.99-1.02)</td>
<td>0.53</td>
</tr>
<tr>
<td>Fick CI</td>
<td>0.56 (0.44-0.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PAC</td>
<td>0.92 (0.84-1.0)</td>
<td>0.037</td>
</tr>
<tr>
<td>RV function</td>
<td>1.18 (1.06-1.31)</td>
<td>0.0019</td>
</tr>
<tr>
<td>eGFR</td>
<td>0.99 (0.98-0.99)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

When PAC was exchanged for PVR in this model, the p-value of PVR was 0.69.
## Results

### Baseline Characteristics of treatment cohort

<table>
<thead>
<tr>
<th></th>
<th>Treatment Cohort (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 ± 13</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>78</td>
</tr>
<tr>
<td>Ischemic Etiology (%)</td>
<td>47</td>
</tr>
<tr>
<td>Left Ventricular EF (%)</td>
<td>24 ± 13</td>
</tr>
</tbody>
</table>
### Results

#### Hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>Treatment Cohort (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline Hemodynamic Data</td>
</tr>
<tr>
<td>Heart Rate Baseline (bpm)</td>
<td>87 ± 18</td>
</tr>
<tr>
<td>Mean arterial pressure Baseline (mmHg)</td>
<td>82 ±13</td>
</tr>
<tr>
<td>Mean RA pressure Baseline (mmHg)</td>
<td>18 ± 6</td>
</tr>
<tr>
<td>Mean PA pressure Baseline (mmHg)</td>
<td>43 ± 9</td>
</tr>
<tr>
<td>PCWP Baseline (mmHg)</td>
<td>31 ± 7</td>
</tr>
<tr>
<td>Fick Cardiac index Baseline (L/min/m²)</td>
<td>1.84 ± 0.64</td>
</tr>
</tbody>
</table>
## Results

### Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Treatment Cohort (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor or ARBs (%)</td>
<td>72</td>
</tr>
<tr>
<td>Beta-blockers (%)</td>
<td>72</td>
</tr>
<tr>
<td>Loop diuretics (%)</td>
<td>99</td>
</tr>
<tr>
<td>Aldosterone antagonists (%)</td>
<td>56</td>
</tr>
<tr>
<td>Nitroprusside (%)</td>
<td>75</td>
</tr>
<tr>
<td>Hydralazine (%)</td>
<td>74</td>
</tr>
<tr>
<td>Isosorbide Dinitrate (%)</td>
<td>66</td>
</tr>
<tr>
<td>Milrinone (%)</td>
<td>28</td>
</tr>
<tr>
<td>Dobutamine (%)</td>
<td>24</td>
</tr>
</tbody>
</table>
Results

A.

Pulmonary capacitance (ml/mmHg)

PVR (mmHg - sec/ml)

PCWP = 16 ± 5

PCWP = 31 ± 7

B.

Pulmonary arterial time constant (sec)

Before Treatment

After Treatment

p < 0.0001
Conclusions

1. In left sided heart failure the pulmonary arterial time cte $\tau$ decreases with increasing PCWP

Conclusions

2. In left sided heart failure, pulmonary arterial capacitance (PAC) has superior prognostic ability compared to pulmonary vascular resistance (PVR) because it incorporates
   – Inverse hyperbolic relationship with PVR
   – Inverse linear relationship with PCWP
Conclusions

3. Treatment of decompensated left-sided heart failure decreases pulsatile load (by increasing capacitance) more than resistive load.
Limitations

• Retrospective study
• Echocardiography was not done at the same time of the catheterization (30 days)
• RV dysfunction was subjective
Inferences

• If interested in prognosis of heart failure patients PAC > PVR
• PVR retains its importance in certain situations (e.g. transplant eligibility)
• Elevated left sided filling pressures increase pulsatile load on the RV
Thanks

- Wilson W. H. Tang, MD
- Yuping Wu
- Wilfried Mullens, MD
- David O. Taylor, MD
- Randall C. Starling, MD, MPH
It is unclear which afterload parameter:
- Best explains RV failure
- Has the highest prognostic significance

**3-element Windkessel**
- Peripheral resistance $R$
- Arterial compliance $C$
- Characteristic impedance $Z$

- Pulmonary Vascular Resistance (PVR)
  \[ R + Z = \frac{\text{mean PA} - \text{PCWP}}{\text{CO}} \]
- Pulmonary Arterial Capacitance (PAC)
  \[ = C = \text{Stroke volume/pulse pressure} \]
Back-up

*In Pulmonary Arterial Hypertension*

- $PVR \times PAC = \tau = Cte$ \(^1\)

\[ \begin{align*}
\Delta C_A \\
\Delta C_B \\
\Delta R \\
R
\end{align*} \]

- PAC as higher prognostic significance \(^2\)

Back-up

PCWP <= 10 mmHg; n=3315
PCWP >= 20 mmHg; n=1584
SPH/PH cohort

$y = 0.577 / (0.048 + x); R^2 = 0.41$

$y = 0.306 / (0.031 + x); R^2 = 0.33$

$RC = -0.0063 \cdot PCWP + 0.46$

$R^2 = 0.98, p<0.002$