Clinical Experience with Pressure Sensor Based Autoregulation of Blood Flow in an Artificial Heart

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Disclosures

• Carmat TAH is an investigational device, not available in the USA

• Carmat SA employee
Why Carmat TAH?

- To provide **Physiological Heart Replacement Therapy** for patients with end stage heart failure*
  - Biventricular failure or risk for RV failure if treated with LVAD
  - Treatment-refractory malignant arrhythmias
  - Restrictive or constrictive etiology (hypertrophic, amyloidosis)

- To address shortcomings of current TAH / bi-ventricular support options
  - Poor hemocompatibility
  - Poor QOL
  - Poor flow regulation
  - Poor pulsatility (BiVAD)
  - Aortic insufficiency (BiVAD)

LVAD: recurring issue of failure of the unassisted right ventricle

- Failure of the right ventricle in patients treated with LVAD:
  - 6-month incidence: 10%*
  - 24-month incidence: 32%**

- Associated with other undesirable events: congestion, impaired renal function, hepatic impairment, infection

* Netuka I et al., J Am Coll Cardiol 2015;66:2579–89
Carmat: Physiological Heart Replacement Therapy

- Pulsatile
- Biventricular
- Hemocompatible
- Auto-regulated
How does the device work?

**Principle:**

Volumetric pumps move the silicone oil within the bag to activate the hybrid membranes allowing the blood to enter and leave the chambers.

**Mode of operation:**

1 – **Blood flow assessment:**
Preload measured by pressure sensors every millisecond to calculate flow required.

2 – **Flow auto-regulation:**
Speed and direction of rotation of volumetric pumps adapted every 2 milliseconds to deliver the necessary pulsatile flow.

3 – **Flow Control:**
Position of the membranes checked by 2 ultrasound sensors every 2 milliseconds to ensure full ejection at every beat, to avoid stasis in blood compartment.
Controller/monitor + batteries
Autonomy at least 4 hours at 6 l/min
Implantation Technique

TEE: de-airing/weaning
**Autoregulation**

- **Objective**
  - Automatically adapt flow to patient needs

- **Two main parameters**
  - RV filling pressure (target = 0)
  - Delta L-R filling pressure (target = 0)
Autoregulation initiated after CPB weaning
First Clinical Experience with Autoregulation

RESEARCH CORRESPONDENCE

Effects of pre-load variations on hemodynamic parameters with a pulsatile autoregulated artificial heart during the early post-operative period

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Study Design

• Objectives
  – Evaluate variation in cardiac output in response to preload changes
  – Evaluate the need for device settings change

• Methods
  – First 10 patients cohort of the CE Mark study, representing a cumulative support duration of 1,947 days (5.3 years).
  – Device data log analysis

• Endpoint
  – Number of device setting changes during clinical course
### Patient Characteristics and Clinical Course

- 8/10 patients were discharged from ICU; median time to discharge 8 days
- 7/10 patients were discharged from hospital; median time to discharge 53 days
- Longest duration (ongoing) 16 months

<table>
<thead>
<tr>
<th>Age</th>
<th>60 (35-70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>4 IHD, 6 DCM</td>
</tr>
<tr>
<td>Indication</td>
<td>6 BTT/BTC, 4 DT</td>
</tr>
<tr>
<td>INTERMACS</td>
<td>All 2 or 3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Day 1</th>
<th>Day 7</th>
<th>M1</th>
<th>M3</th>
<th>M6</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAP (mmHg)</td>
<td>28±5</td>
<td>10±3</td>
<td>11±6</td>
<td>Catheter not in place</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>15±5</td>
<td>10±3</td>
<td>12±6</td>
<td>Catheter not in place</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>99±10</td>
<td>105±16</td>
<td>110±12</td>
<td>117±13</td>
<td>114±7</td>
<td>125±23</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>66±5</td>
<td>57±7</td>
<td>60±11</td>
<td>68±12</td>
<td>75±8</td>
<td>79±6</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>2.9±0.7</td>
<td>5.7±0.6</td>
<td>5.9±0.8</td>
<td>6.1±0.7</td>
<td>5.9±0.6</td>
<td>6.1±0.6</td>
</tr>
</tbody>
</table>
Device settings change

- Device settings were changed 20 times in 10 patients, during 5.3 pt.yrs observation
  - 65% occurred in the first month (ICU),
  - 90% of the changes were done on 1 setting (RV admission pressure)
  - Only 1 change was needed after hospital discharge
- With experience, less changes were performed
Hemodynamic Performance

No device settings change
Exercise-induced flow changes

![Graph showing flow changes over time with markers for T0 Spirometer time and Stop Spirometer time. The graph indicates fluctuations in flow with distinct time markers and labels for Left Flow and Charge.]
## Clinical Outcome and Safety Profile

### Comparative outcomes 10 cases - 6 months follow up

<table>
<thead>
<tr>
<th></th>
<th>Survival rate</th>
<th>Bleeding – surgical repair</th>
<th>Stroke</th>
<th>Gastrointestinal bleeding</th>
<th>Driveline infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARMAT</td>
<td>70%</td>
<td>40%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>SynCardia*</td>
<td>54% - 62%</td>
<td>41%</td>
<td>23%</td>
<td>20%</td>
<td>22%</td>
</tr>
<tr>
<td>BIVAD**</td>
<td>46% - 68%</td>
<td>n/a</td>
<td>7%</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>LVAD***</td>
<td>90% - 92%</td>
<td>14%</td>
<td>8%</td>
<td>8%</td>
<td>10%</td>
</tr>
</tbody>
</table>


Conclusions

• Carmat automatic flow regulation is controlled effectively by preload-sensitive algorithm
• Autoregulated flow results in immediate and durable hemodynamic recovery
• Autoregulation: « Start and Forget »
• Autoregulation provides the hemodynamic condition for positive safety profile and improved quality of life
Merci Beaucoup!

67 y/o man, DT indication, 16 months on Carmat