Mechanical Circulatory Devices: Contemporary Long-Term Management

Do Patients Need a Pulse?

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Do LVAD Patients Need a Pulse?

• Features of new continuous flow ventricular assist devices (CVAD) have increased their use as long-term treatment for advanced heart failure
  • Small size
  • High durability and reliability

• Concerns exist over the impact of sustained, “non-pulsatile” circulatory support.

• The debate over the role of pulse pressure has been complicated by:
  • Inconsistencies and inaccuracies in quantifying pulsatility
  • Variations in VAD operation
  • CVAD-associated clinical risks
  • Lack of long-term studies
Pulsatility

• Traditional quantifications of pulsatility:
  • Based on pressure (aortic pressure, $AoP$):
    \[ \text{Pulse Pressure} = AoP_{\text{max}} - AoP_{\text{min}} \]
  • Based on blood velocity ($V$):
    \[ \text{Pulsatility Index (PI)} = \frac{V_{\text{max}} - V_{\text{min}}}{V_{\text{mean}}} \]

• Criticisms of these traditional measurements:
  • Pressure and velocity are considered independently and individually.
  • They do not adequately quantify pulsatility of VAD-generated “non-physiologic” flows.
Pulsatility

• Pulsatile flow is a function of hemodynamic energy gradient over time:
  • Interaction of flow and pressure
  • The entire cardiac beat, not just minimum/maximum points

• More accurate measures for pulsatility:
  • Energy Equivalent Pressure (EEP)

\[
EEP = \frac{\int f \cdot P \, dt}{\int f \, dt} , \quad f = \text{instantaneous flow} \quad P = \text{instantaneous pressure}
\]

• Relative change between EEP and mean arterial pressure (MAP)
  • i.e. Surplus Hemodynamic Energy

\[
SHE \ [\text{erg/cm}^3] = 1332 \times (EEP - MAP)
\]

• EEP and SHE are rarely used clinically.
Role of Pulse

- Initial successes of CVAD have put into question the necessity of a pulse.
- The “pulse” of the heart allows time for ventricular filling and cardiac muscle contraction.
  - “Pulse” time is not required with CVAD support.
- The pulse provides critical mechanical stimuli to vascular tissue.
  - Regulates many signaling cascades:
    - Vascular tone
    - Inflammation,
    - Proliferation, etc.

![Diagram showing pressure pulse, pulsatile/oscillatory shear stress, and circumferential cyclic stretch.](image)
Role of Pulse

- However, pulse pressure immediately begins to be attenuated by arterial compliance.
  - Arguably negligible at the capillary-level
- What is the long-term impact of diminished hemodynamic pulsatility?

A.R. Travis, et al., 2007
Surplus Hemodynamic Energy: CF vs PF

Pulsatility and VADs
Slaughter et al JHLT 2013

• Pulsatile flow (PVAD) and current Continuous flow (CVAD) VADs have different affects on blood flow pulsatility.
  • PVAD can augment pulsatility
  • CVAD can only attenuate pulsatility
Emerging CF VAD Technologies

- Remaining uncertainties over “non-pulsatile” flow
  - Introduce and optimize pulsatility with CVAD
Preliminary Data
Vascular Remodeling

Relative Collagen Content

<table>
<thead>
<tr>
<th>Condition</th>
<th>Blue : Red Pixel Ratio</th>
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<tbody>
<tr>
<td>Normal</td>
<td>0.3 ± 0.05</td>
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<tr>
<td>IHF n=4</td>
<td>0.7 ± 0.05</td>
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<tr>
<td>Chronic LVAD n=4</td>
<td>0.8 ± 0.05</td>
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Images show histological sections with 100 µm markers.
Speed Modulation Profiles

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pressure (mmHg)</th>
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<tbody>
<tr>
<td>IHF Baseline</td>
<td>27±1</td>
</tr>
<tr>
<td>Constant Speed</td>
<td>14±4</td>
</tr>
<tr>
<td>Copulse</td>
<td>16±3</td>
</tr>
<tr>
<td>Counterpulsed</td>
<td>10±3</td>
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<tr>
<td>Asynchronous Modulation</td>
<td>19 - 25</td>
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Mean pulse pressures (High RPS)
Ex Vivo Arterial Perfusion

1. Mock circulation loop
2. CF LVAD
3. Ex vivo perfusion chamber with bovine artery
   • Benefits of this approach
     • Uses LVAD to generate experimental fluid flow
     • Includes effects of native ventricular ejection with LVAD
Preliminary Data – Ex Vivo Culture

Bovine carotid arteries with H&E staining (4x magnification) show preserved morphology at (a) 0-hour, (b) 14-hour, (c) 24-hour, and (d) 48-hour time points.
Interactions with the microvasculature

A. Thickness of SMC Layer of the Arterioles. Representative □SMA immunostaining of LV tissue. a, pulsatile-flow LVAD pre-implantation. b, pulsatile-flow LVAD post-removal. c, continuous-flow LVAD pre-implantation. d, continuous-flow LVAD post-removal. Tissue samples collected at pre-implantation and post-removal were stained and evaluated simultaneously using the same sample carrier. e, Thickness of smooth muscle cell layer; □SMA, □ smooth muscle actin.

Saito T et al. Artif Organs. 2017
Effects of LVAD modulation on arterial pressure waveforms

![Waveform Diagram](image)

**Fig. 1** Arterial blood pressure waveforms and blood flow in the common carotid artery (CCA) and middle cerebral artery (MCA) of representative healthy and left ventricular assist device (LVAD) patients. **a** In the healthy circulation, blood pressure and CCA blood flow are pulsatile, which is somewhat reduced but still clearly present in the MCA. **b** HeartMate II with low pump speed has a moderately reduced pulse pressure and pulsatility. **c** HeartMate II with high pump speed has significantly reduced pulse pressure and pulsatility. **d** Jarvik 2000 with transition from high to low pump speed occurring every 2 s (0.15 s of reduced speed by 2000 rpm below baseline and 0.20 s of increased speed by 2000 rpm above baseline), also termed “artificial pulse”

Effects of LVAD speed modulation in HF

Figure 3  Sample left ventricular pressure-volume loops recorded in a chronic ischemic heart failure (IHF) bovine model without pump support (IHF Baseline), during constant speed (rpm), and during speed modulation profiles (synchronous copulse, synchronous counterpulse, and asynchronous) with an HVAD (HeartWare, Miami Lakes, FL) continuous-flow left ventricular assist device.

Soucy KG et al. J Heart Lung Transplant. 2015
Do LVAD Patients Need a Pulse

• Yes – need to define what are our goals
  standard pulse pressure
  maintaining EEP and SHE
  pulse pressure that maintains endothelial function
  clinical pressure that reduces adverse events

• Reducing pump speed to allow aortic valve to open and create pulse
  not ideal in most settings

• It will be possible to have flow modulation in the future that could
  meet our goals
George Bernard Shaw
1856-1950

Thank You

“Science is always wrong. It never solves a problem without creating ten more.”