Optimization of Hemodynamics in Mechanical Circulatory Support Patients

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Disclosures

• I have no relevant financial disclosures or conflicts of interest.
• We will be discussing off-label applications of medical devices.
Learning Objectives

• Understand the impact of various mechanical circulatory support (MCS) approaches on cardiac pressure-volume relationships.
• Describe the role of left ventricular unloading with veno-arterial MCS.
• Summarize the importance of recognizing biventricular failure.
• Manage hemodynamic alterations associated with veno-venous extracorporeal membrane oxygenation.
Important Caveat

• MCS devices and approaches vary significantly
• Clinical substrate is markedly heterogeneous
• No two MCS patients are alike
Quick Review
Left-Sided Mechanical Circulatory Support
Generally Speaking...

Three common left-sided support configurations:

• Right atrium or central venous circulation → systemic artery
  • Veno-arterial MCS (i.e. VA ECMO)

• Left atrium → systemic artery (i.e. aorta)
  • TandemHeart (trans-septal cannulation)

• Left ventricle → systemic artery (i.e. aorta)
  • Implanted
    • Left-ventricular assist devices
  • Percutaneous
    • Impella
    • (HeartMate PHP)
RA → Ao

- Baseline:
  - High LVEDP
  - Low pressure generation
  - Low stroke volume
  - Low EF
- As we increase flow:
  - Increased LV afterload
  - Increased effective arterial elastance (Ea)
Sequelae of LV Overload

• Pulmonary edema
• Prolonged, or thwarted, recovery
  • Impaired remodeling
  • Wall stress
  • Increased myocardial oxygen consumption
• Hypercoagulability
Unloading the LV

- Manipulation of peripheral resistance
  - Baroreceptors
  - Pharmacologically
    - Vasodilators
    - Flow adjustment
  - Mechanically
    - IABP

D Burkhoff et al. J Am Coll Cardiol. 2015
Unloading the LV

- Improve LV function
  - Increased coronary perfusion (Ao pressure)
  - Normalize myocardial oxygen delivery
- Normalize acid/base
- Inotropes

D Burkhoff et al. J Am Coll Cardiol. 2015
<table>
<thead>
<tr>
<th>Location or procedure</th>
<th>Mechanisms of unloading</th>
<th>Efficacy of venting (grade from ✓ to ⬤)</th>
<th>Cost &amp; Complexity (grade from ✓ to ⬤)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricle</td>
<td>LV unloading (direct with catheter in the cardiac apex or through the mitral valve from the left atrium)</td>
<td>⬤</td>
<td>⬤</td>
</tr>
<tr>
<td>Interatrial septostomy (septostomy usually with ballooning or stent)</td>
<td>Left-to-right atrial shunt</td>
<td>✓</td>
<td>⬤</td>
</tr>
<tr>
<td>Left atrium (transeptal or interatrial groove, or left atrial roof, or right superior pulmonary vein catheter or cannula attached to the ECMO venous return or to device like TandemHeart®)</td>
<td>Left atrial unloading (indirect LV and pulmonary venous unloading)</td>
<td>⬤</td>
<td>(✓✓✓✓✓ with device)</td>
</tr>
<tr>
<td>Trans-aortic (catheter or device like Impella®)</td>
<td>LV unloading</td>
<td>⬤</td>
<td>(✓✓✓✓✓ with device)</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>Increased right-side blood drainage (indirect pulmonary venous and left cardiac chamber unloading)</td>
<td>✓</td>
<td>⬤</td>
</tr>
<tr>
<td>Systemic vein (femoral, jugular, subclavian) or right atrium</td>
<td>Increased right-side blood drainage (indirect pulmonary venous and left cardiac chamber unloading)</td>
<td>✓</td>
<td>⬤</td>
</tr>
<tr>
<td>IABP</td>
<td>Reduced LV afterload (enhanced systolic ejection) and reduced LV end-diastolic pressure (enhanced left atrial and pulmonary venous unloading)</td>
<td>✓</td>
<td>⬤</td>
</tr>
</tbody>
</table>

LV, left ventricular; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.
**Figure 2** Location of LV Unloading. LV, Left Ventricle; LA, left atrium; IABP, Intra-Aortic Balloon Pump; PA, pulmonary artery.
Should We?
The Effect of Intraaortic Balloon Pumping Under Venoarterial Extracorporeal Membrane Oxygenation on Mortality of Cardiogenic Patients: An Analysis Using a Nationwide Inpatient Database

Shotaro Aso, MD, MPH¹; Hiroki Matsui, MPH¹; Kiyohide Fushimi, MD, PhD²; Hideo Yasunaga, MD, PhD¹
Figure 1. Patient selection. IABP = intraaortic balloon pumping, VA-ECMO = venoarterial extracorporeal membrane oxygenation.
Figure 2. Survival plots for patients applied to venoarterial extracorporeal membrane oxygenation with or without intraaortic balloon pumping. IABP = intraaortic balloon pumping, VA-ECMO = venoarterial extracorporeal membrane oxygenation.
Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock

Federico Pappalardo¹†*, Christian Schulte²†, Marina Pieri¹, Benedikt Schrage², Rachele Contri³, Gerold Soeffker⁴, Teresa Greco¹, Rosalba Lembo¹, Kai Müllerleile²,
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total (n = 63)</th>
<th>ECMO + Impella (n = 21)</th>
<th>ECMO (n = 42)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality, n (%)</td>
<td>41 (65)</td>
<td>10 (48)</td>
<td>31 (74)</td>
<td>0.04</td>
</tr>
<tr>
<td>Bridge to next therapy or recovery, n (%)</td>
<td>28 (44)</td>
<td>13 (62)</td>
<td>15 (36)</td>
<td>0.048</td>
</tr>
<tr>
<td>Weaning from MCS, n (%)</td>
<td>26 (41)</td>
<td>10 (48)</td>
<td>16 (28)</td>
<td>0.047</td>
</tr>
<tr>
<td>Bridge to recovery, n (%)</td>
<td>19 (30)</td>
<td>8 (38)</td>
<td>11 (26)</td>
<td>0.3</td>
</tr>
<tr>
<td>Bridge to VAD, n (%)</td>
<td>8 (13)</td>
<td>4 (19)</td>
<td>4 (9.5)</td>
<td>0.5</td>
</tr>
<tr>
<td>Bridge to cardiac transplantation, n (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Duration of ECMO, h</td>
<td>120 (36–234)</td>
<td>148 (72–239)</td>
<td>73.5 (29–217)</td>
<td>0.2</td>
</tr>
<tr>
<td>Duration of MV, h</td>
<td>93 (29–228)</td>
<td>163 (90–228)</td>
<td>48 (17–265)</td>
<td>0.04</td>
</tr>
<tr>
<td>CVVH, n (%)</td>
<td>18 (29)</td>
<td>10 (48)</td>
<td>8 (19)</td>
<td>0.02</td>
</tr>
<tr>
<td>Haemolysis, n (%)</td>
<td>30 (48)</td>
<td>16 (76)</td>
<td>14 (33)</td>
<td>0.004</td>
</tr>
<tr>
<td>Major bleeding, n (%)</td>
<td>20 (32)</td>
<td>8 (38)</td>
<td>12 (29)</td>
<td>0.6</td>
</tr>
<tr>
<td>Minor bleeding, n (%)</td>
<td>14 (22)</td>
<td>4 (19)</td>
<td>10 (24)</td>
<td>0.8</td>
</tr>
<tr>
<td>LVEF at weaning, %</td>
<td>45.5 (30–55)</td>
<td>52.5 (47–55.5)</td>
<td>37.5 (25–50)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

CVVH, continuous veno-venous haemofiltration; MCS, mechanical circulatory support; MV, mechanical ventilation; VAD, ventricular assist device.
Unloading the LV on VA ECMO

• Is less more?

• If...
  • Lactate kinetics are favorable
  • Myocardial function stable or improving
  • End-organ perfusion OK

• Consider...
  • Turning down flows and accepting a lower MAP

• What about inotropes?
LA $\rightarrow$ Ao

- **TandemHeart**
  - 21 Fr trans-septal inflow cannula
  - Centrifugal pump
  - Arterial outflow cannula (typically 15-19 Fr)

- Blood withdrawn directly from LA
LA $\rightarrow$ Ao

- As we increase flow:
  - LV decompresses
  - LV EDP decreases
  - LV performance improves
LA $\rightarrow$ Ao

- These relationships change as peripheral resistance and end-systolic elastance vary.
LV $\rightarrow$ Ao

- Impella
  - Catheter mounted, impeller driven, axial flow pump
  - Driven across the aortic valve
  - Impella 2.5: 12 Fr
  - Impella CP: 14 Fr
  - Impella 5.0: 21 Fr
- Anchoring catheter
- Hemolysis is a common complication
LV $\rightarrow$ Ao

- As flow increases...
  - Loss of isovoluemic periods
  - Pressure-volume loop changes shape
  - Progressive LV unloading (left-shifted loop)
  - Arterial and left ventricular pressures uncouple

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LV $\rightarrow$ Ao

• These relationships change as peripheral resistance and end-systolic elastance vary
Right-Sided Mechanical Circulatory Support
Generally Speaking...

Two common right-sided support configurations:

- Indirect RV bypass (RA $\rightarrow$ Ao)
  - VA ECMO
- Direct RV bypass (RA $\rightarrow$ PA)
  - Impella RP
  - TH Protek Duo
  - Assorted RVAD configurations
Device Flow (Q) = \frac{\text{RPMs}}{H} = \frac{\text{RPMs}}{\text{Pout} - \text{Pin}} \\
\text{(PA)} \quad \text{(RA)}

Pulmonary Hypertension
H = \text{PA (50/30)} - \text{RA (20)}

Acute RV Failure
H = \text{PA (30/20)} - \text{RA (20)}
Direct RV Bypass

Recognizing Biventricular Failure

Figure 7. Proposed algorithm for right ventricular (RV) acute mechanical circulatory support (AMCS) device use in RV failure. LV indicates left ventricular; PA, pulmonary artery; RVAD, right ventricular assist device; RVMI, right ventricular myocardial infarction; VA-ECMO, venoarterial extracorporeal membrane oxygenation; and VT/VF, ventricular tachycardia/ventricular fibrillation. *Unresponsive defined by new or persistent systolic blood pressure <90 mm Hg or cardiac index <2.2 requiring ≥1 inotrope or vasopressor worsening end-organ perfusion.
Recognizing Biventricular Failure

- **Right-sided support (RA → PA) with LV dysfunction**
  - LV volume overload
  - → LV pressure overload
  - Acute pulmonary edema
  - Worsened RV function

- **Left-sided support (LA/LV → Ao) with RV dysfunction**
  - Impaired LV preload
  - → LV suction
Veno-Venous ECMO
ECMO Biomaterial with absorbed proteins

Contact Activation
- C3
- C3a
- C3b
- C3bBb
- Anaphylatoxins

Complement Activation
- C5
- C5a
- C6, C7, C8, C9

Coagulation Cascade
- HMWK
- Bradykinin
- Contact Factors

Fibrinogen
- Thrombin
- Prothrombin

Platelet Degranulation
- IL-1β
- TNF-α

Neutrophil Activation
- Complement Products
- Thrombin and FXIIa

Platelet Activation
- Endothelial Activation
- Neutrophil Extravasation

Endothelium
- Integrins
- Pro-inflammatory cytokines
- P-selectin and other adhesion molecules

<table>
<thead>
<tr>
<th></th>
<th>VV ECMO</th>
<th>CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>Days to weeks</td>
<td>Minutes to hours</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>+/- low dose heparin</td>
<td>High-dose heparin</td>
</tr>
<tr>
<td>Reversal of anticoagulation</td>
<td>Rarely</td>
<td>Protamine</td>
</tr>
<tr>
<td>Hemodilution</td>
<td>Minimal</td>
<td>Deliberate</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Air-blood interface</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Pulsatility</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ischemia-reperfusion</td>
<td>Variable</td>
<td>Yes</td>
</tr>
</tbody>
</table>
VV ECMO and SIRS

• Contact system
  • Kallikrein and bradykinin mediated (immediate)

• Intrinsic/extrinsic coagulation
  • Prothrombin $\rightarrow$ thrombin via FXa; mediated via biocompatible circuits

• Complement system
  • Immunomodulatory response leading to inflammation (delayed – hours)

• Endothelial cells
  • Inflammatory mediators lead to pro-inflammatory cytokine production and glycoxalyx injury

• Leukocytes
  • Neutrophils and monocytes are activated by extracorporeal circulation

• Platelets
  • Multiple proinflammatory interactions (delayed – days)
Management

• Important to differentiate SIRS from infection/sepsis
  • Prolonged vasogenic shock is not necessarily a marker of infection
  • Use procalcitonin to guide decisions

• Vasopressors to manage SIRS, not volume
  • Vasopressors also recruit unstressed venous volume and may help avoid the need for fluids

• Reduce concomitant causes of inflammation
  • Rest the lungs
  • Renal replacement therapy
  • Treat infection

• Future frontiers: the microcirculation
Thank You!

Questions?

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