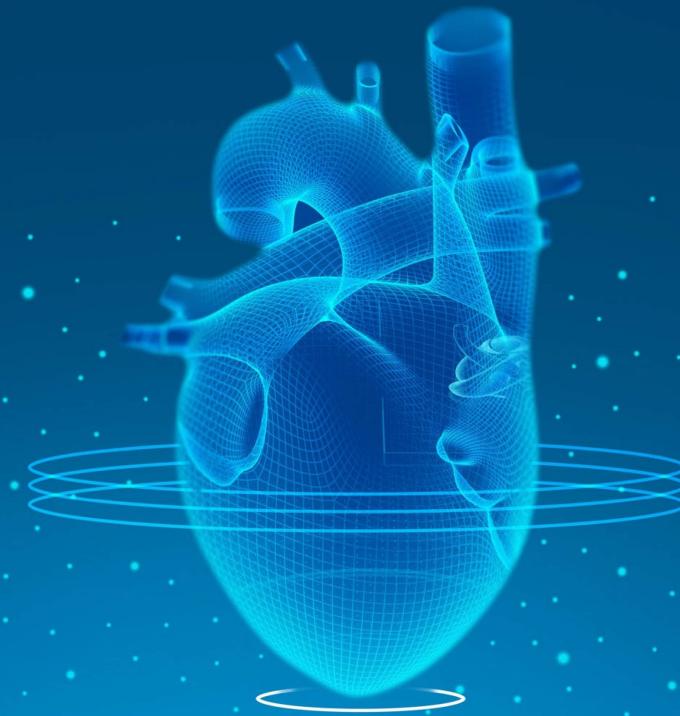
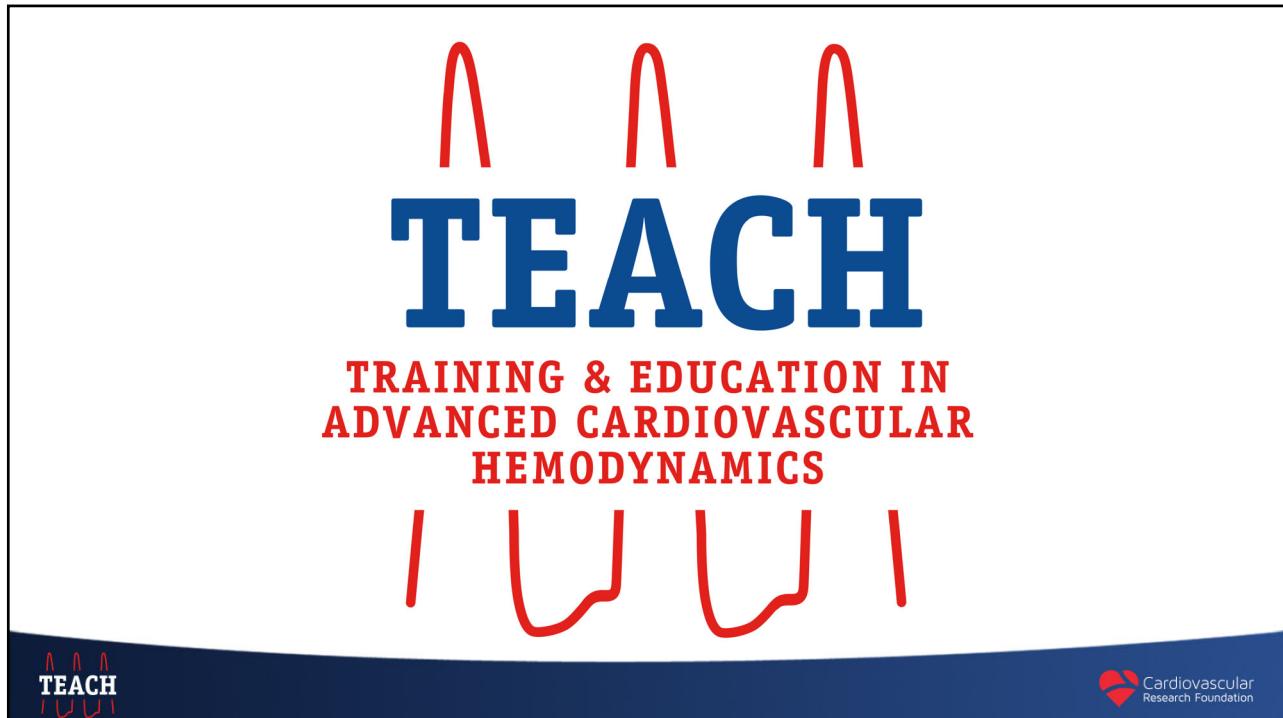




GRAND ROUNDS





1

The Pathophysiology of Cardiogenic Shock and the Hemodynamic Effects of Different forms of Mechanical Circulatory Support

Daniel Burkhoff MD PhD

Director

Heart Failure, Hemodynamics and Mechanical Circulatory Support Research

Cardiovascular Research Foundation

New York, NY



2

Disclosures

- Unrestricted institutional educational grant from Abiomed
- Consultant to PVLoops LLC



3

Learning Objectives

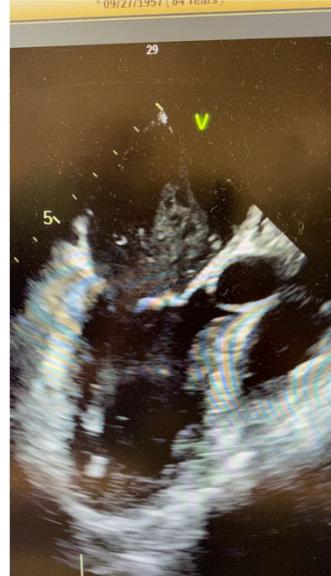
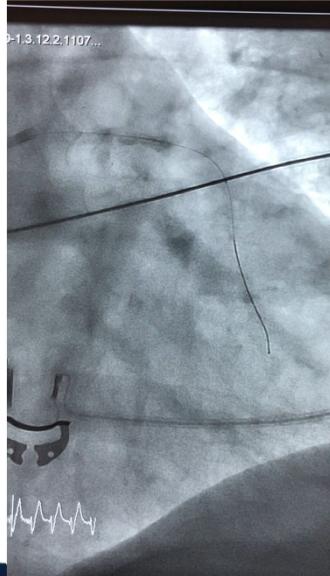
At the conclusion of this talk, you should be able to:

1. Explain the impact of elevated CVP on mortality in patients with cardiogenic shock due to acute myocardial infarction and in cardiogenic shock due to decompensated chronic heart failure
2. Compare the primary hemodynamic and metabolic effects of a percutaneous left ventricular assist device and ECMO circuit in the setting of cardiogenic shock
3. Explain why the hemodynamic response to any form of mechanical circulatory support differs among patients
4. Explain why some patients require LV unloading during ECMO support and at least 8 ways this can be treated



4

Courtesy of Dr. Manreet Kanwar. Allegheny General Hospital



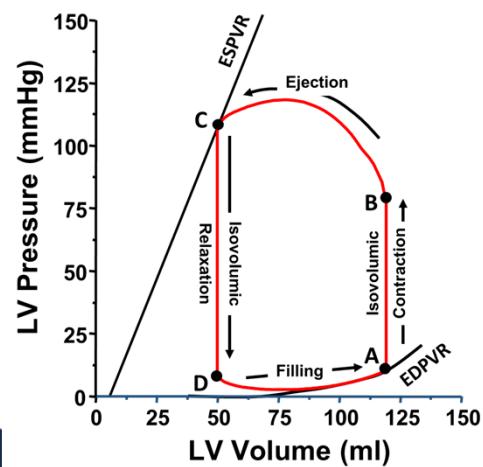
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5

Understanding Ventricular-Vascular Coupling through the Window of the Pressure-Volume Diagram:

Ventricular Pressure-Volume Loop
End-Systolic Pressure-Volume Relationship
End-Diastolic Pressure-Volume Relationship

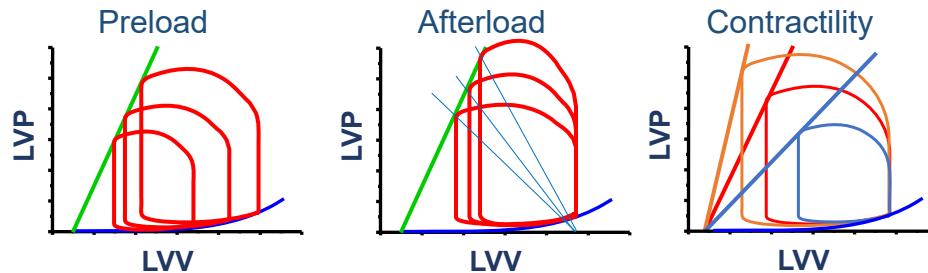


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Ventricular-Vascular Coupling: Overview



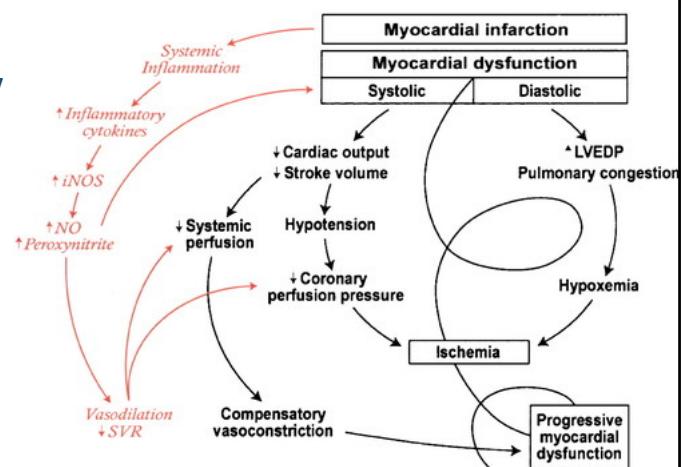
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7

Pathophysiology of CS

- Primary insult of the myocardium
- Primary effects of \downarrow LV, \downarrow RV or \downarrow BiV contractility
- Results in:
 - \downarrow BP, \downarrow CO, $\uparrow/\downarrow/\leftrightarrow$ CVP and PCWP, acidemia
- Secondary, effects of baroreceptor activation (rapid)
 - \uparrow HR,
 - \uparrow SVR,
 - Venoconstriction \rightarrow \uparrow stressed blood volume (SBV)
- Longer term:
 - Inflammation, MOF



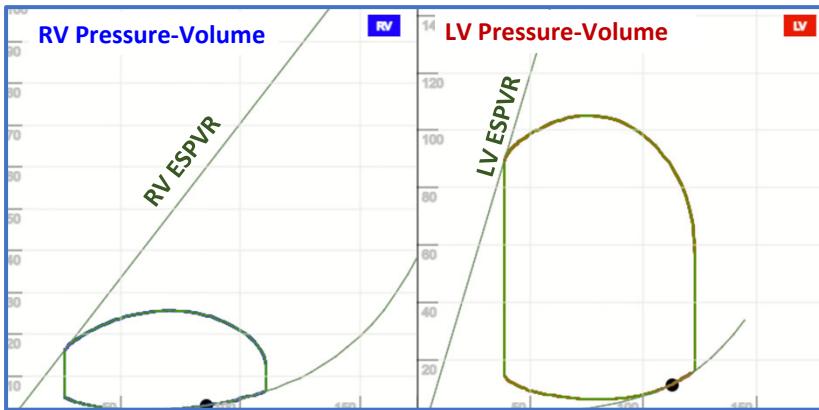
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Hochman 2003

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8

Pressure-Volume Relations in Shock due to Isolated LV Failure



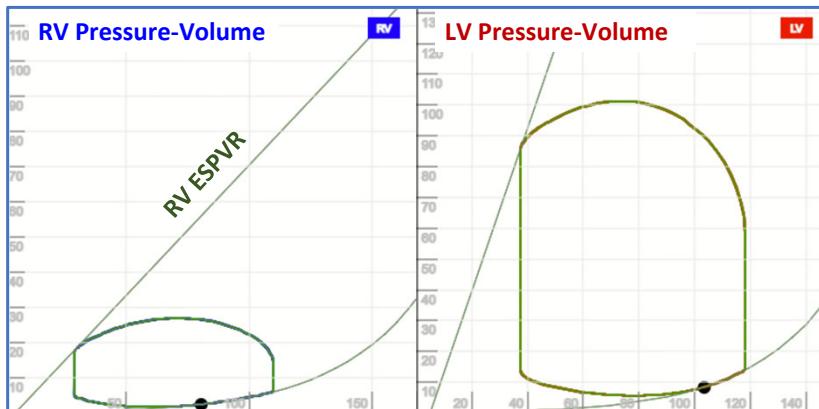
- Abrupt reduction of LV contractility
- Decreased BP and CO
- Baroceptor activation increases HR, SVR and stressed blood volume (SBV)
- PCWP increase
- Variable changes of CVP

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Pressure-Volume Relations in Shock due to Isolated RV Failure



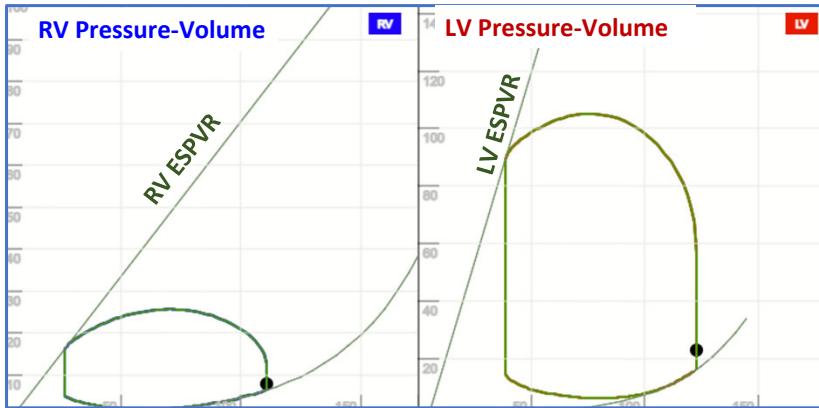
- Abrupt reduction of RV contractility
- LV underfilling leads to decreased CO and BP
- Baroceptor activation increases HR, SVR and SBV
- CVP increases
- Variable changes of PCWP

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10

Pressure-Volume Relations in Shock due to Acute Biventricular Failure



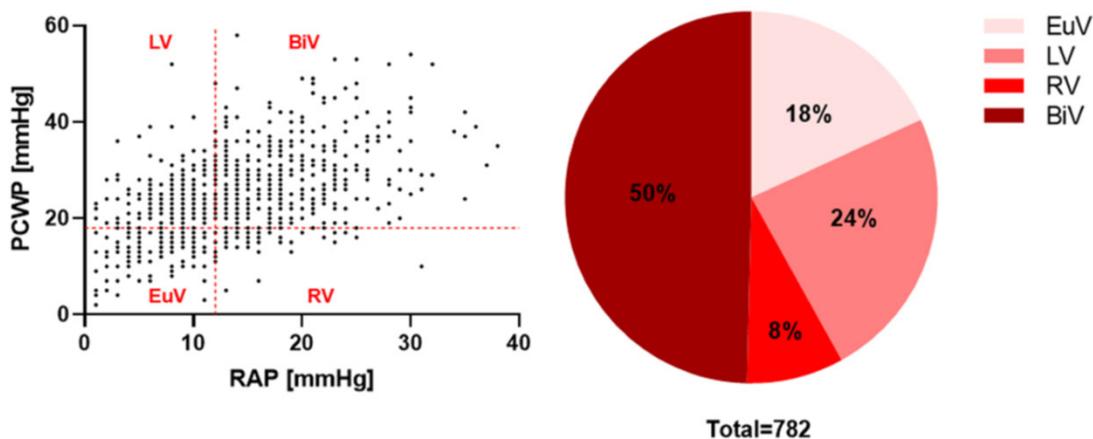
- Reductions of both LV and RV contractilities
- Decreased BP and CO
- Baroceptor activation increases HR, SVR and stressed blood volume
- Variable changes of CVP and PCWP

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11

Invasive Hemodynamic Assessment and Classification of In-Hospital Mortality Risk Among Patients With Cardiogenic Shock



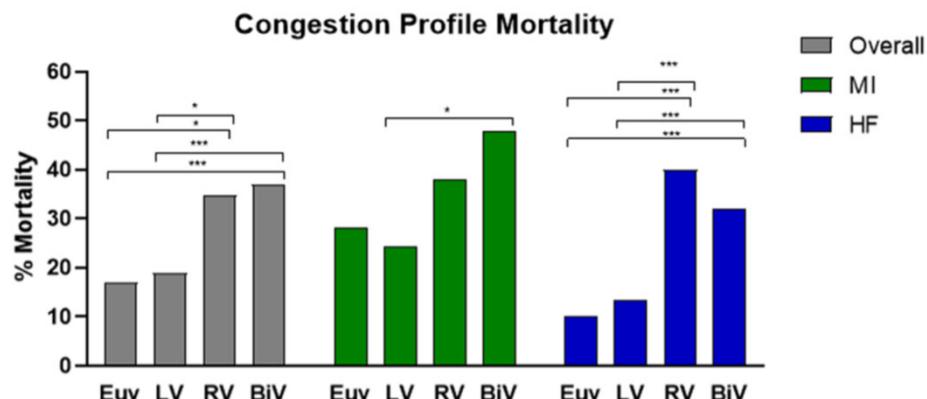
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Thayer, et al., Circ Heart Fail. 2020;13:e007099

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Invasive Hemodynamic Assessment and Classification of In-Hospital Mortality Risk Among Patients With Cardiogenic Shock



Thayer, et al., Circ Heart Fail. 2020;13:e007099



13

Therapeutic Options

- Pharmacology
 - Inotropic agents
 - Pressors
- Devices
 - IABP
 - RA → Ao (ECMO)
 - LA → Ao (Tandem)
 - LV → Ao (Impella)
 - ECMO + Impella



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KEY POINT

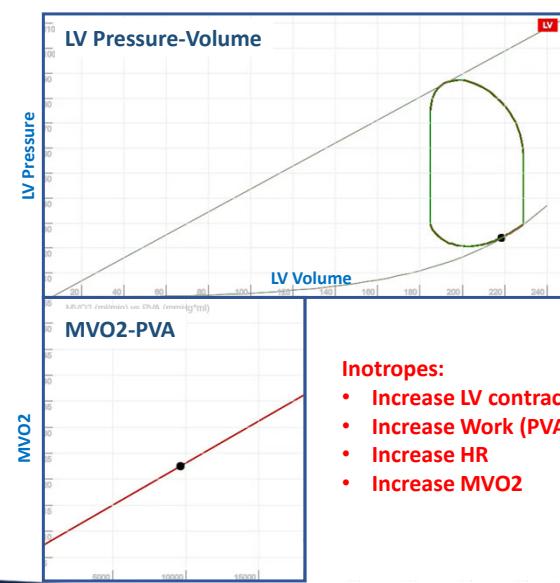
Hemodynamic response to device and drug therapies variable among patients due to baseline characteristics and secondary effects:

- Degree of LV and/or RV compromise
- Short term recoverability of LV/RV function
- SVR and PVR
- Volume Status
- MR / TR
- Background medical therapy
- Other...



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Impact of Inotropes/Pressors on LV Mechanics and Energetics



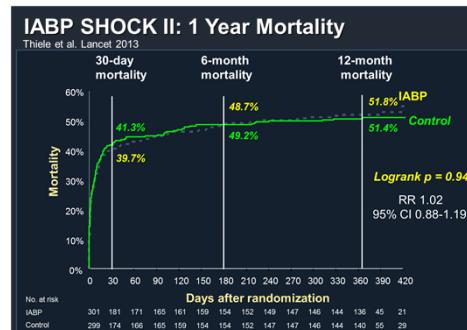
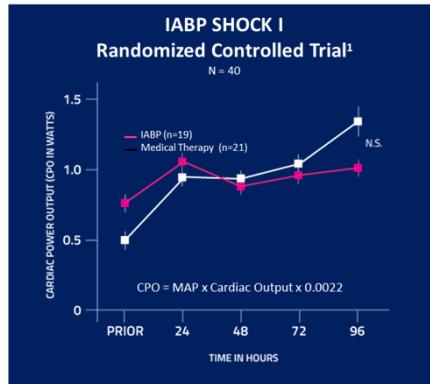
- Inotropes can:
- Increase CO
 - Increase BP

- Inotropes:**
- Increase LV contractility
 - Increase Work (PVA)
 - Increase HR
 - Increase MVO₂



16

Intraaortic Balloon Pump: No significant effects on hemodynamics (CPO) or mortality



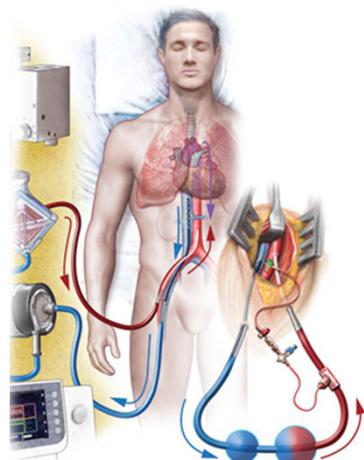
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17

VA-ECMO RA → FA

Peripheral Cannulation



Venoarterial Extracorporeal Membrane Oxygenation in Cardiogenic Shock.
Keebler ME ... Lindenfeld J. JACC Heart Fail. 2018

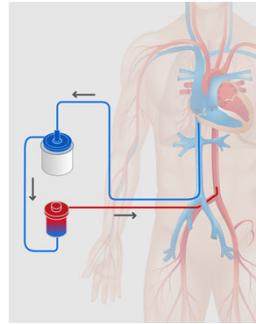
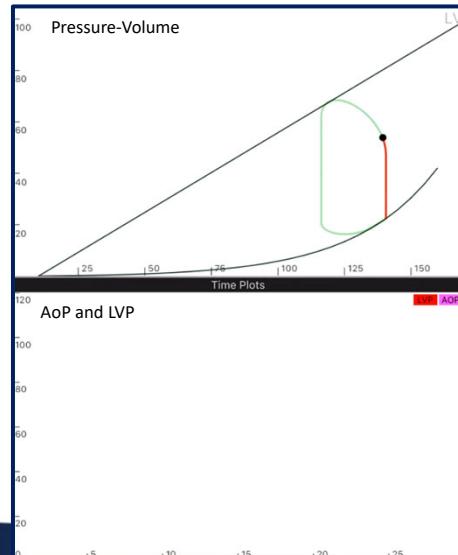
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Impact of RA → Ao MCS (ECMO) on Hemodynamics and Energetics

**↑ Afterload
↑ Preload**

**↑ AoP
↑ LVP**



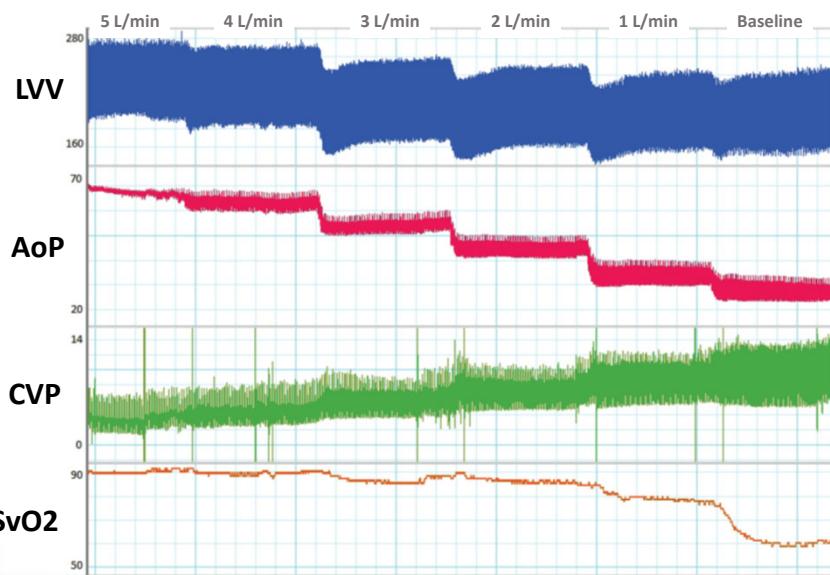
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Regional Tissue Oximetry Reflects Changes in Arterial Flow in Porcine Chronic Heart Failure Treated With Venoarterial Extracorporeal Membrane Oxygenation

Hala et al, Physiol Res 2016;65:S621-632

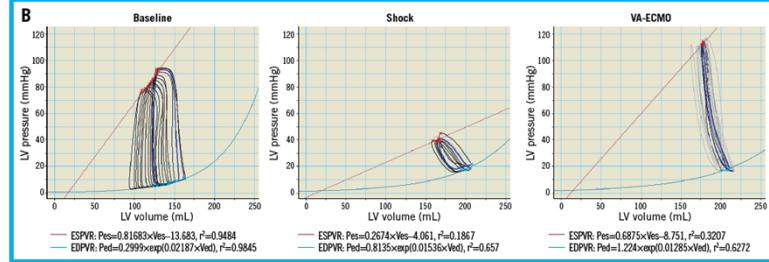


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20

VA-ECMO in Profound Cardiogenic Shock



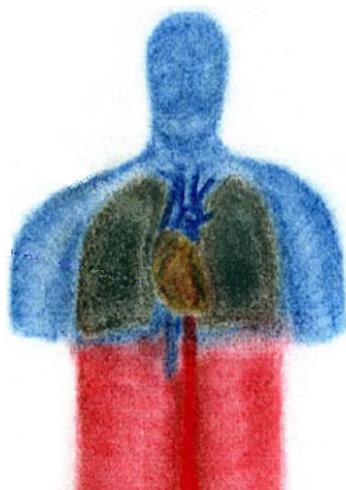
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Møller-Helgestad et al.
EuroIntervention 2019;14:e1585-e1592



21

Harlequin Syndrome / North-South Syndrome



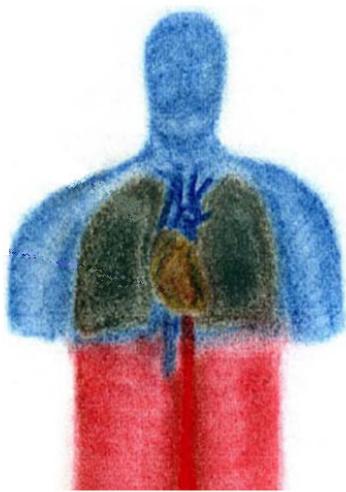
Harlequin:
a mute character in traditional
pantomime, typically masked and
dressed in a diamond-patterned
costume

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22

Harlequin Syndrome / North-South Syndrome

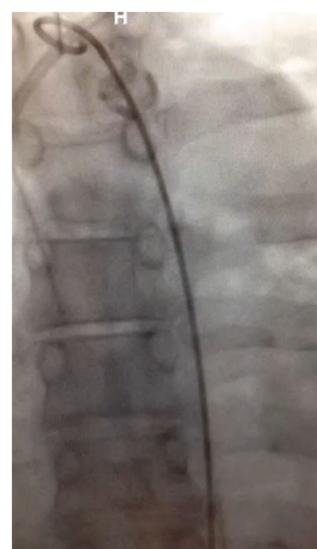
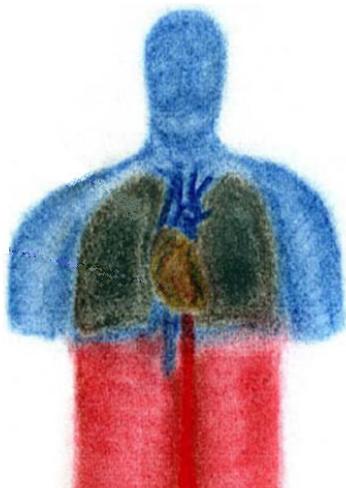


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Harlequin Syndrome / North-South Syndrome

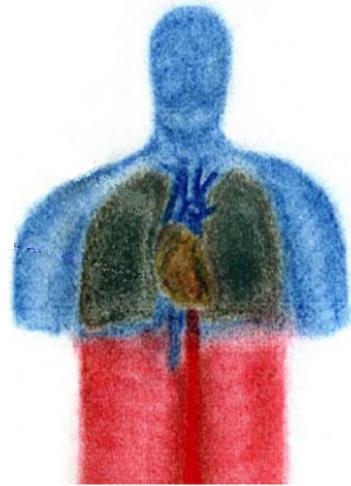


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Harlequin Syndrome / North-South Syndrome



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25

LV Distention and Pressure Overload during ECMO Support

- Loss of aortic valve opening
- Lung edema
- Bronchial bleeding
- LV thrombosis

Courtesy of Dr. Jiri Maly, IKEM, Prague



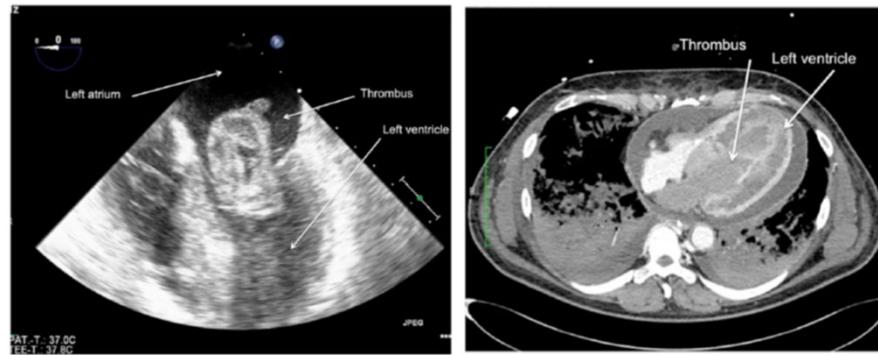
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Left ventricular thrombus formation in patients undergoing femoral veno-arterial extracorporeal membrane oxygenation

Weber et al, Perfusion 2017



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Patient on ECMO Courtesy of Dr Sal Monnino



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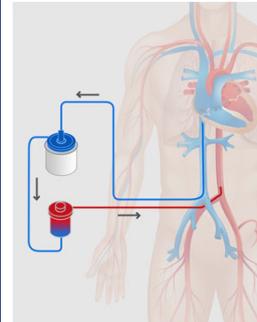
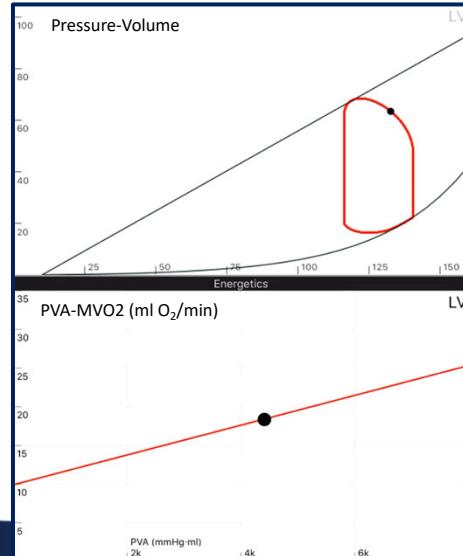
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Impact of RA→Ao MCS (ECMO) on Hemodynamics and Energetics

**↑ Afterload
↑ Preload**

**↑ PVA
↑ MVO₂**



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KEY POINT

Hemodynamic response to device and drug therapies variable among patients due to baseline characteristics and secondary effects:

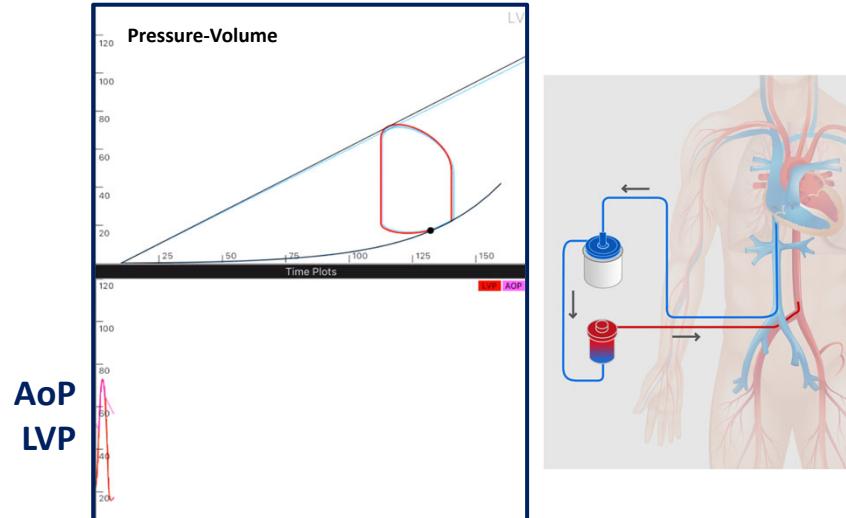
- Degree of LV and/or RV compromise
- Short term recoverability of LV/RV function
- SVR and PVR
- Volume Status
- MR / TR
- Background medical therapy
- Other...

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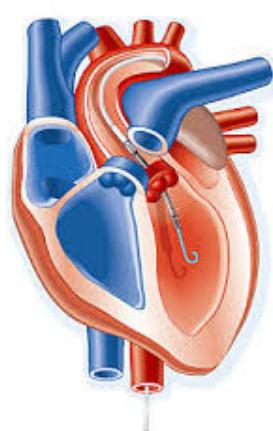
Impact of RA → Ao ECMO in CGS with LV Contractile Reserve



31



Percutaneous Transvalvular Pumps



Impella Family of Devices
2.5/4.0/5.0/RP

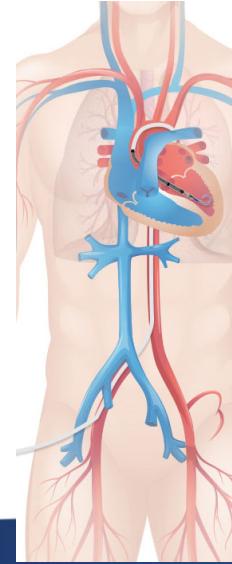
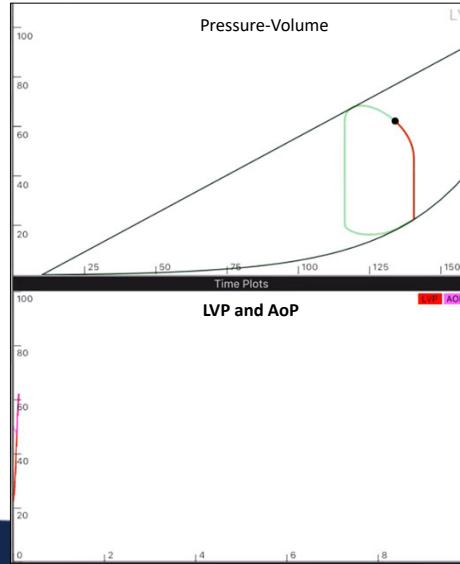


32

Impact of LV→Ao MCS on Hemodynamics and Energetics

\downarrow Peak LVP
 \downarrow Preload

\uparrow AoP
 \downarrow LVP
LV-Ao Uncoupling



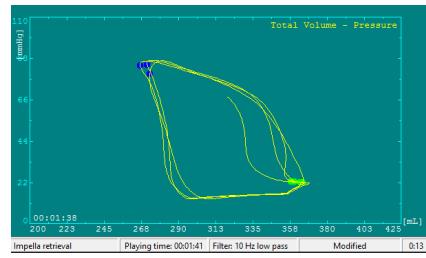
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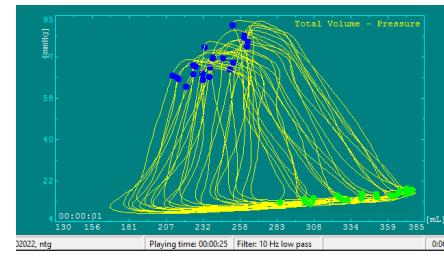
HRPCI under IMPELLA support Courtesy of William O'Neill

REAL PV Loops assume triangular shape during LVAD Support

Impella Removed from LV



PV Loops during Impella support and NTG injection

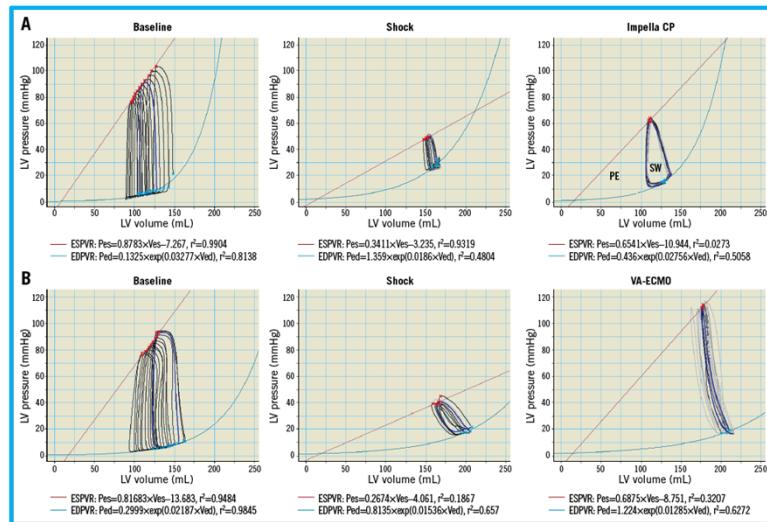


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Impella CP or VA-ECMO in Profound Cardiogenic Shock



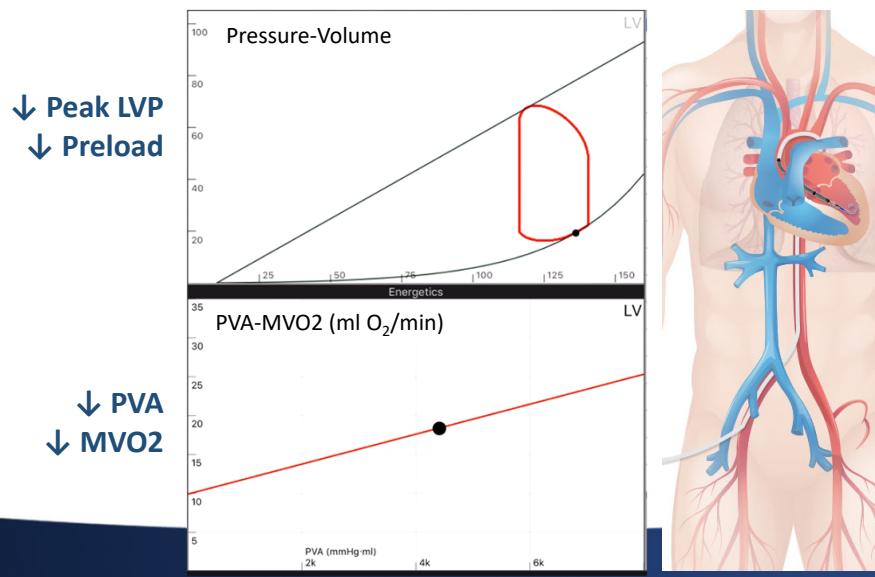
Møller-Helgestad et al.

EuroIntervention 2019;14:e1585-e1592



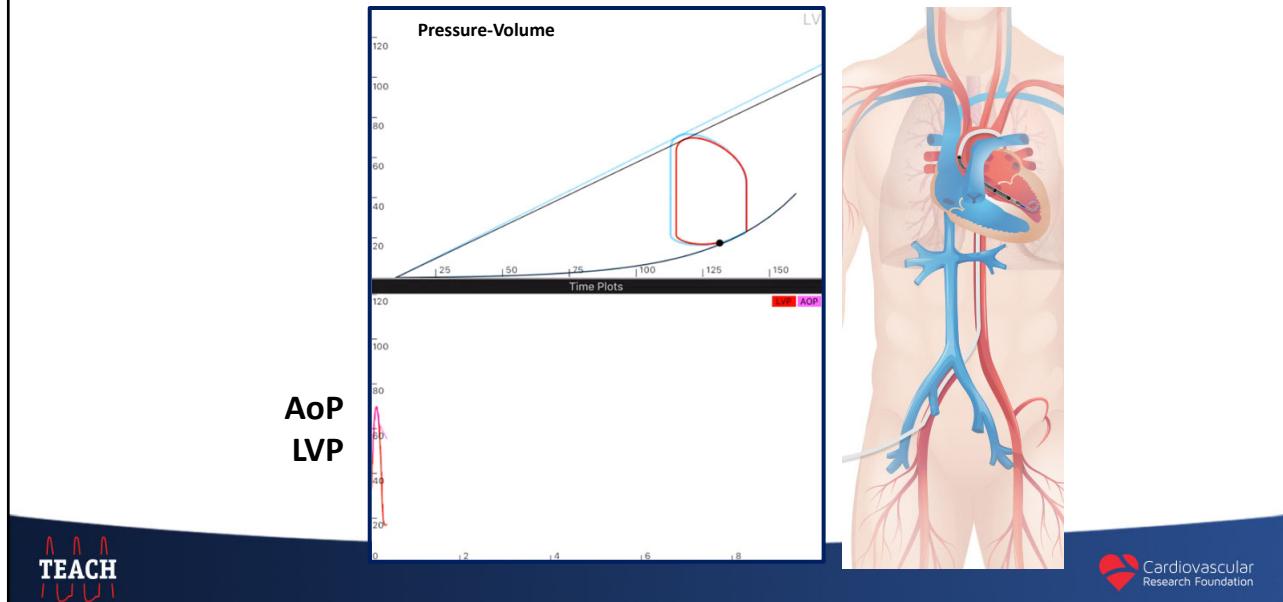
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Impact of LV → Ao MCS on Hemodynamics and Energetics



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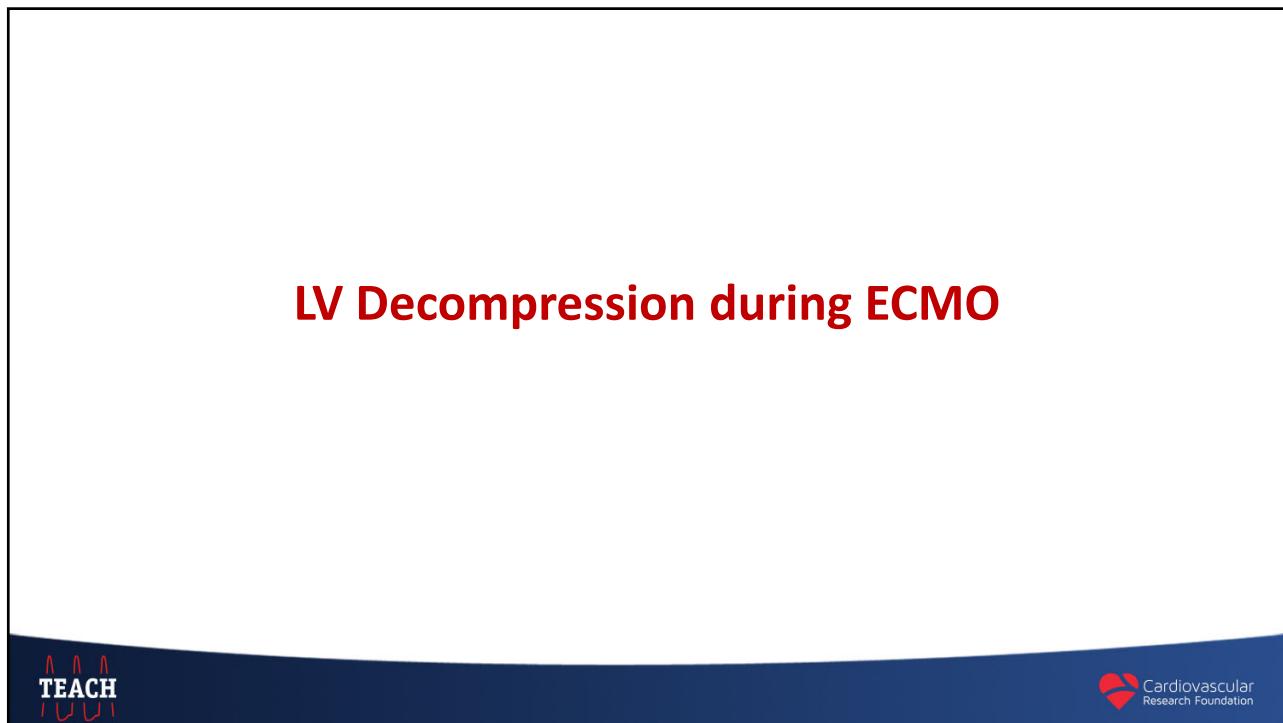
Impact of LV→Ao in CGS with LV Contractile Reserve



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LV Decompression during ECMO



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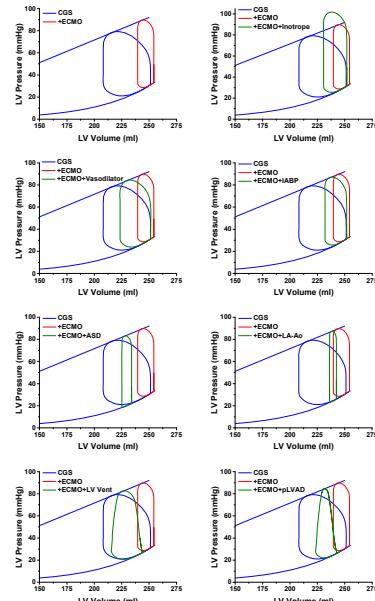
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Venoarterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock and Cardiac Arrest

Cardinal Considerations for Initiation and Management

Rao, Khalpey, Smith, Burkhoff and Kociol
CircHF 2018

1. Reduce ECMO speed
2. Inotropes
3. Afterload reduction (e.g., nitroprusside)
4. IABP
5. Atrial Septostomy
6. LA → FA bypass (TandemHeart)
7. LV Vent
8. LV → Ao pump (e.g., Impella)

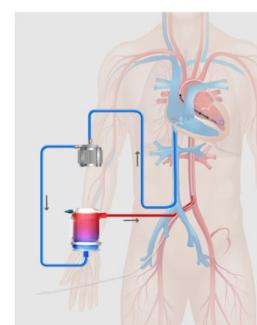
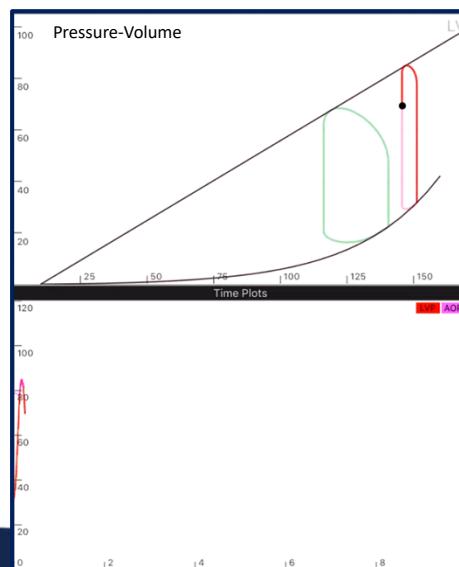


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RA → Ao MCS + LV → Ao MCS

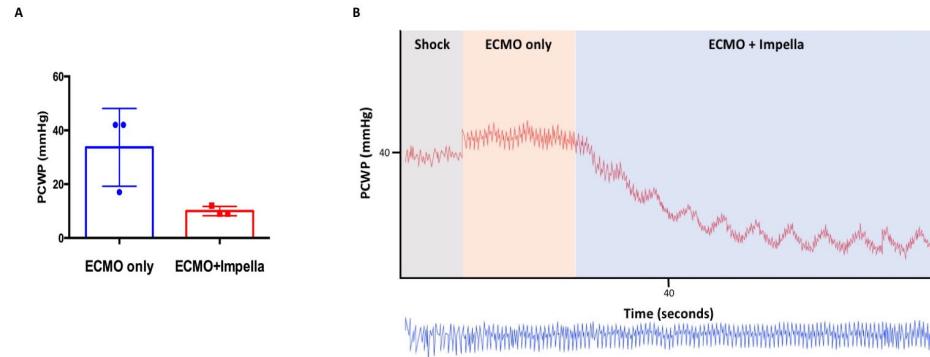
↑ Afterload
↑ Preload

AoP
LVP



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Rapid and Marked Reduction of PCWP with Impella added to ECMO



Schrage et al, JACC:HF, in press



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The Effect of Impella CP on Cardiopulmonary Physiology During Venoarterial Extracorporeal Membrane Oxygenation Support

HS Lim, Artificial Organs, 2017; 41:1109

TABLE 2. Hemodynamic changes pre- and post-Impella on VA-ECMO support

| | VA-ECMO | VA-ECMO + Impella | P |
|--------------------------|-------------------|-------------------|--------|
| Inotrope score | 25.3 ± 3.9 | 24.8 ± 3.5 | 0.811 |
| HR (min^{-1}) | 122 ± 7 | 111 ± 6 | 0.015 |
| MAP (mm Hg) | 60 ± 5 | 63 ± 3 | 0.109 |
| SV (mL) | 17.0 ± 1.9 | 31.8 ± 4.3 | <0.001 |
| PASP (mm Hg) | 44.7 ± 4.3 | 36.0 ± 5.2 | 0.011 |
| PADP (mm Hg) | 29.8 ± 6.0 | 20.8 ± 5.2 | 0.015 |
| Mean PA (mm Hg) | 35.2 ± 5.8 | 27.6 ± 5.7 | 0.046 |
| PAWP (mm Hg) | 26.5 ± 6.7 | 17.5 ± 4.3 | 0.020 |
| PCap (mL/mm Hg) | 1.16 ± 0.10 | 2.15 ± 0.61 | 0.002 |
| PVR (mm Hg/mL/s) | 0.25 ± 0.03 | 0.17 ± 0.04 | 0.001 |
| RC (s) | 0.289 ± 0.026 | 0.360 ± 0.036 | 0.002 |



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Summary

1. Understanding cardiac physiology in the framework of the ventricular PV domain helps explain the hemodynamics of CGS and therapeutics
 - a. ECMO
 - b. Percutaneous LVAD
2. Responses to devices vary among patients
3. Percutaneous LVADs directly unload the LV while decreasing PCWP and increasing blood flow to the body
4. VA ECMO has the potential to increase the load on the LV and reduce AoV opening (LV and Ao root stasis)
5. At least 8 approaches to LV unloading
 - a. Important to know advantages and limitations of each



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