The Pathophysiology of Cardiogenic Shock
Knowledge Gaps & Opportunities

Navin K. Kapur, MD, FACC, FSCAI, FAHA
Associate Professor, Department of Medicine
Interventional Cardiology & Advanced Heart Failure Programs
Executive Director, The Cardiovascular Center for Research & Innovation
Relevant Disclosures

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NIH  American Heart Association  American Stroke Association
life is why

HFSA

Herbert J. Levine Foundation
Tufts Medical Center

Charlton Award
Tufts Medical Center

RO1HL139785, RO1H133215
Which Cardiogenic Shock Are We Talking About?

AMI-Shock
- 10/2007
- Anterior MI
- LAD PCI and IABP
- LVEF 20%

AMI-Shock
- 11/2007
- Readmitted
- Heart Failure
- LVEF 25%

ACUTE HF SYNDROMES
- 11/2007
- Readmitted - HF
- ICD Implanted
- LVEF 25%

HR-PCI
- 3/2008
- Readmitted
- Recurrent HF
- LVEF 25%
- 4/2009
- Readmitted – HF/ACS
- Impella Supported
- LAD and LCx PCI
- LVEF 25%

Advanced HF-Shock
- 12/2017
- Cardiogenic Shock
- Impella + VA-ECMO
- LVEF 10%

Advanced HF-Shock
- 12/2017
- Cardiogenic Shock
- Biventricular Centrimags
- LVEF 10%

Orthotopic Heart Transplant
- 4/2018
- LVEF 65%

Ambulatory Shock
- 7/2012
- Readmitted
- Recurrent HF
- LVEF 20%

Ambulatory Shock
- 3/2015
- Readmitted
- Recurrent HF
- LVEF 20%
Which Cardiogenic Shock Are We Talking About?

Acute MI Cardiogenic Shock

Advanced HF Cardiogenic Shock

Modified from Goodlin. JACC 2009;54:386
Our Current Understanding of CGS Physiology
Founded in AMI-Shock

Coronary Problem

Ventricular Failure

Vascular Response

AHA Shock Consensus Statement Circ 2017
Primary Target of Heart Failure Therapy: Reduce LV Wall Stress

Laplace’s Law: Wall stress = \( \frac{\text{Pressure} \times \text{Radius}}{2 \times \text{Wall Thickness}} \) = \( \frac{\text{ESP} \times \text{EDV}}{\text{LV Mass}} \)
Plumbing 101: Ventricular ‘Loading’ Conditions

Arterial Elastance (Ea)

\[ Ea = \frac{ESP}{SV} \]

End-Systolic Elastance (Ees) Contractility

Afterload = Wall Stress = ESP x EDV

Pressure

Volume

Potential Energy

Stroke Volume

Stroke Work
Plumbing 201: Ventriculo-Arterial Coupling

Arterial Elastance ($E_a$) vs. Volume

End-Systolic Elastance ($E_{es}$) vs. Contractility

Ventriculo-Arterial Coupling = $\frac{E_a}{E_{es}}$

Potential Energy

Stroke Volume

Stroke Work

Volume
How Does Preload Impact the Failing Heart?

Condition 1: ‘Normal’
Condition 2: AMI
Condition 3: Compensated HFrEF
Condition 4: Cardiogenic Shock (AMI or HFrEF)
Inefficient VA-Coupling & Increased Wall Stress in Shock

\[ \frac{E_a}{Ees} = 1 \]

\[ \frac{E_a}{Ees} \gg 1 \]
Afterload:
1. Resistance
2. Impedance
3. PA compliance
4. PA elastance

Plumbing 301: RV-PA Coupling

Pulm. Arterial Hypertension

Courtesy of HC Champion
Effect of elevated pulmonary capillary wedge pressure (PCWP) on pulmonary vascular resistance-compliance relationship (RPA-CPA).


Plumbing 401: RV-PA-LV Coupling

PCWP = \frac{\text{PA Compliance}}{\text{PA Resistance}}

Plumbing 401: RV-PA-LV Coupling

Condition 1: ‘Normal’
Condition 2: AMI
Condition 3: Acute Heart Failure
Condition 4: Cardiogenic Shock

Stroke Volume vs. LVEDP or LVEDV

Normal

CHF

LV Capacitance & Stroke Volume

LV Capacitance & Stroke Volume
Message 1: CGS is a Biventricular Problem

Hemodynamic Indices of RV Failure

A. CVP > 16
B. RA:PCWP > 0.6 or > 0.8
C. RVSW < 450
D. PAPi (PAPP/CVP) < 1.0

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### Left Anterior Descending Artery

<table>
<thead>
<tr>
<th>Heart rate (beats/min)</th>
<th>103.2 ± 22.6 (122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td>13.5 ± 5.8 (53)</td>
</tr>
<tr>
<td>PAS (mm Hg)</td>
<td>38.9 ± 11.7 (77)</td>
</tr>
<tr>
<td>PAD (mm Hg)</td>
<td>23.7 ± 8.0 (76)</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>23.4 ± 9.4 (106)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.11 ± 0.69 (74)</td>
</tr>
<tr>
<td>CPI (W/m²)</td>
<td>0.33 ± 0.13 (71)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>26.5 ± 9.6 (55)</td>
</tr>
<tr>
<td>Median SVR (dyne s/cm²)</td>
<td>1,121 [838, 1,366] (40)</td>
</tr>
</tbody>
</table>

### Left Circumflex Artery

<table>
<thead>
<tr>
<th>Heart rate (beats/min)</th>
<th>106.5 ± 24.2 (37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td>16.5 ± 5.8 (15)</td>
</tr>
<tr>
<td>PAS (mm Hg)</td>
<td>41.0 ± 9.4 (20)</td>
</tr>
<tr>
<td>PAD (mm Hg)</td>
<td>24.5 ± 6.9 (20)</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>26.3 ± 7.3 (33)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.42 ± 0.83 (24)</td>
</tr>
<tr>
<td>CPI (W/m²)</td>
<td>0.37 ± 0.15 (24)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>30.0 ± 11.1 (21)</td>
</tr>
<tr>
<td>Median SVR (dyne s/cm²)</td>
<td>1,165 [978, 1,807] (10)</td>
</tr>
</tbody>
</table>

### Right Coronary Artery

<table>
<thead>
<tr>
<th>Heart rate (beats/min)</th>
<th>91.5 ± 23.0 (77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td>16.4 ± 6.0 (32)</td>
</tr>
<tr>
<td>PAS (mm Hg)</td>
<td>37.3 ± 10.8 (48)</td>
</tr>
<tr>
<td>PAD (mm Hg)</td>
<td>22.8 ± 6.2 (48)</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>23.2 ± 7.7 (66)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.12 ± 0.87 (49)</td>
</tr>
<tr>
<td>CPI (W/m²)</td>
<td>0.34 ± 0.16 (43)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>38.7 ± 14.4 (33)</td>
</tr>
<tr>
<td>Median SVR (dyne s/cm²)</td>
<td>1,199 [679, 1,435] (19)</td>
</tr>
</tbody>
</table>

### Left Main Artery

<table>
<thead>
<tr>
<th>Heart rate (beats/min)</th>
<th>96.9 ± 22.9 (16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrial pressure (mm Hg)</td>
<td>22.5 ± 11.0 (4)</td>
</tr>
<tr>
<td>PAS (mm Hg)</td>
<td>53.4 ± 12.5 (5)</td>
</tr>
<tr>
<td>PAD (mm Hg)</td>
<td>31.7 ± 11.7 (6)</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>33.5 ± 11.2 (11)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>1.60 ± 0.54 (7)</td>
</tr>
<tr>
<td>CPI (W/m²)</td>
<td>0.29 ± 0.15 (6)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>30.2 ± 17.8 (5)</td>
</tr>
<tr>
<td>Median SVR (dyne s/cm²)</td>
<td>1,782 [1,782, 1,782] (1)</td>
</tr>
</tbody>
</table>

| RA:PCWP | 0.6     | 0.64   | 0.71   | 0.67   |
| PAPi     | 1.0     | 0.97   | 0.91   | 0.98   |

Fincke JACC 2004
Message 1: CGS is a Biventricular Problem

### Hemodynamic Variables of Right Ventricular Function

<table>
<thead>
<tr>
<th>Variable</th>
<th>RV Dysfunction</th>
<th>RV failure</th>
<th>Recover Right Trial Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVP</td>
<td>&gt;10 mmHg</td>
<td>&gt; 15 mmHg</td>
<td>CVP</td>
</tr>
<tr>
<td>CVP/PCWP</td>
<td>&gt;0.63</td>
<td>&gt;0.8</td>
<td>CVP/PCWP</td>
</tr>
<tr>
<td>PAPi</td>
<td>&lt;2.0</td>
<td>&lt;1.5</td>
<td>Cardiac Index</td>
</tr>
<tr>
<td>RVSWI</td>
<td>&lt;450</td>
<td>&lt;300</td>
<td>Inotrope / Pressor</td>
</tr>
</tbody>
</table>

SHOCK Registry: 30-Day Mortality

- RV Failure: 48% in SHOCK Trial (n=140), 51% in SHOCK Registry (n=260)
- RV Dysfunction: 37% in SHOCK Trial (n=140), 37% in SHOCK Registry (n=260)
- No RV Dysfunction: 12% in SHOCK Trial (n=140), 15% in SHOCK Registry (n=260)

Recovery Right Trial Criteria Met?

- YES: 80%
- NO: 70%

p=0.03
The Cardiogenic Shock Working Group

Total: 1010 Cases

- No AMCS
- IABP only
- Impella CP
- Impella RP
- Impella 5.0
- CP + RP
- Impella 5.0 + RP
- VA ECMO
- VA ECMO + Impella CP
- Other

Largest US registry of Acute MCS device use in Cardiogenic Shock
Over 500 patients with PA Catheter Indices
Message 1: CGS is a Biventricular Problem

Biventricular Congestion in Cardiogenic Shock is Common and Associated with High In-Hospital Mortality
Message 2: Congestion is as Critical as Cardiac output

Hemodynamic Predictors of Heart Failure Morbidity and Mortality: Fluid or Flow?

LAUREN B. COOPER, MD,1,2 ROBERT J. MENTZ, MD,1,2 SUSANNA R. STEVENS, MS,1 G. MICHAEL FELKER, MD, MHS,1,2 CARLO LOMBARDI, MD,3 MARCO METRA, MD,3 LYNNE W. STEVENSON, MD,4 CHRISTOPHER M. O’CONNOR, MD,1,2 CARMELO A. MILANO, MD,1,5 CHETAN B. PATEL, MD,1,2 AND JOSEPH G. ROGERS, MD1,2

Cardiac Preload, not Cardiac Index, is a Major Determinant of Clinical Outcomes
Message 2: Congestion is as Critical as Cardiac output

Central Venous Congestion Worsens Renal Function in HF

Mullens and Tang JACC 2009
Message 2: Congestion is as Critical as Cardiac output

Venous Congestion Drives Morbidity and Mortality in CS

Right Atrial Pressure is a common denominator for poor outcomes
The prognostic value of the relationship between right atrial and pulmonary capillary wedge pressure in diverse cardiovascular conditions

Douglas Marshall Brinkley Jr., MD\textsuperscript{a,*}, Kalon K.L. Ho, MD, MSc\textsuperscript{b}, Mark H. Drazner, MD, MSc\textsuperscript{c}, Robb D. Kociol, MD\textsuperscript{b}

Right atrial pressure is independently associated with in-hospital mortality
Odds ratio 1.12 per 1mmHg increase (p<0.001)

Should we be utilizing better approaches to reduce biventricular filling pressures in HF?
Message 3: Hemodynamic vs Hemo-Metabolic Shock
Message 3: Hemodynamic vs Hemo-Metabolic Shock

Pre-Shock
Early Shock
Mild Shock

Hemodynamic Shock

Late Shock
Deep Shock
Severe Shock

Hemo-Metabolic Shock

Mortality (%)

Right Atrial Pressure

<14
≥14

0
20
40
60
80
100

0
20
40
60
80
100

p=0.004

p=0.001

Morne & Kapur et al. Shock Working Group
Message 3: Hemodynamic vs Hemo-Metabolic Shock

An Issue of Timing: Diagnosis, Stratification, Therapy

Circulatory Support Systemic Perfusion + Ventricular Support LV/RV Unloading + Coronary Perfusion + Renal & Hepatic Unloading

Mean Arterial Pressure
LV-ESP & EDP Aortic Pulse Pressure
MAP - LVEDP
RA-PA Hemodynamics

Lactate Creatinine
Vent Tachycardia BNP
ST-Changes Troponin/CK-Mb
Creatinine, LFTs, Coagulopathy

Hemodynamic Problem

Recovery
Rx: Hemodynamic Support Circulatory and Ventricular

Time in Cardiogenic Shock

Hemo-Metabolic Problem

Rx: Multi-organ Support Unloading, Ventilator, CVVHD

Death

Kapur and Esposito Curr Cardio Risk 2016
Kapur and Esposito F1000 2017
Message 4: Escalating Pharmacologic Therapy is Futile

- Hemodynamically driven decision making
- Escalating Inotrope/Vasopressor Use

ROC Curve Pressors and In-Hospital Mortality
- AUC 0.838
- p<0.0001
- Optimal cutoff ≥2

Percent Usage

- Neosynephrine
- Norepinephrine
- Vasopressin
- Epinephrine
- Dobutamine
- Milrinone
- Dopamine

p<0.001 Chi square test for trend
Message 5: Hemodynamically Driven Decision Making

CGS Management begins with a PA Catheter

AMI and Cardiogenic Shock Refractory to 1 inotrope/vasopressor

Echocardiogram

Pericardial Disease
- Tamponade

No Pericardial Disease
- No Tamponade

Cardiac Index > 2.2
- Consider non-cardiac origin or intra-cardiac shunt

Cardiac Index < 2.2

+ Severe Aortic Insufficiency
- TH-LVAD

RA<15
- PCWP<18
- Hypovolemia
- Volume Resuscitation

RA<15
- PCWP≥18
- LV-Dominant

RA≥15
- PCWP<18
- RV-Dominant

RA≥15
- PCWP≥18
- BiV-Dominant

+ Hypoxemia or
+ Persistent VT/VF
- VA-ECMO + LV Vent

TH-LVAD

PAPI > 1.0
- Acute RV AMCS (Impella CP) (Impella 5.0) (TH-RVAD)

PAPI < 1.0
- Inotropes Vasodilators Diuresis

PAPI > 1.0
- Acute LV AMCS (Impella CP) (Impella 5.0) (TH-LVAD)

PAPI < 1.0
- Acute BiV AMCS (BiPella) (VA-ECMO + LV Vent) (TH-BiVAD)
Future Directions for the Science of Cardiogenic Shock

Ventricular Load Impacts Myocardial Recovery

Esposito, Zhang, Qiao & Kapur et al JACC 2018
Future Directions for the Science of Cardiogenic Shock

Ventricular Load Impacts Myocardial Recovery
The Pathophysiology of Cardiogenic Shock
Knowledge Gaps & Opportunities

Thank you

nkapur@tuftsmedicalcenter.org