New Horizons in Cardiogenic Shock

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Cedars-Sinai Heart Institute
AMI Shock Mortality Unchanged in > 20 years

US AMI/CGS cases per year\(^1,2\)


74355 78954 78500 79823 80585 82626 86692 89923

High In-Hospital Mortality During AMI Cardiogenic Shock\(^3\)

N = 23,696

Death Rate, %

2000 2001 2002 2003 2004 2005 2006

2. Acute Cardiac Assist Report, Health Research International – August 2015
Randomized Trials Cardiogenic Shock

### Revascularization

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHOCK</td>
<td>1 year</td>
<td>81/152</td>
<td>0.72 (0.54;0.95)</td>
</tr>
<tr>
<td>SMASH</td>
<td>30 days</td>
<td>22/32</td>
<td>0.87 (0.66;1.29)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>103/184</td>
<td>0.82 (0.69;0.97)</td>
</tr>
</tbody>
</table>

### Vasopressors

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOAP-2 (CS subgroup)</td>
<td>28 days</td>
<td>64/145</td>
<td>0.75 (0.55;0.93)</td>
</tr>
<tr>
<td>Unverzagt et al.</td>
<td>30 days</td>
<td>5/16</td>
<td>0.33 (0.11;0.97)</td>
</tr>
</tbody>
</table>

### Inotropes

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unverzagt et al.</td>
<td>30 days</td>
<td>5/16</td>
<td>0.33 (0.11;0.97)</td>
</tr>
</tbody>
</table>

### Glycoprotein IIb/IIIa inhibitors

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRAGUE-18</td>
<td>In-hospital</td>
<td>15/40</td>
<td>1.15 (0.59;2.27)</td>
</tr>
</tbody>
</table>

### NO synthase inhibitors

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRIUMPH</td>
<td>30 days</td>
<td>97/201</td>
<td>1.14 (0.91;1.45)</td>
</tr>
<tr>
<td>SHOCK II</td>
<td>30 days</td>
<td>24/59</td>
<td>1.16 (0.59;2.69)</td>
</tr>
<tr>
<td>Cotter et al.</td>
<td>30 days</td>
<td>4/15</td>
<td>0.40 (0.13;1.05)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>125/275</td>
<td>1.05 (0.85;1.29)</td>
</tr>
</tbody>
</table>

### IABP

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP-SHOCK I</td>
<td>30 days</td>
<td>7/19</td>
<td>1.28 (0.45;3.72)</td>
</tr>
<tr>
<td>IABP-SHOCK II</td>
<td>30 days</td>
<td>119/300</td>
<td>0.96 (0.79;1.17)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>126/319</td>
<td>0.98 (0.81;1.18)</td>
</tr>
</tbody>
</table>

### LVAD

<table>
<thead>
<tr>
<th>Trial</th>
<th>Follow-up</th>
<th>n/N</th>
<th>Relative Risk 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiele et al.</td>
<td>30 days</td>
<td>9/21</td>
<td>0.95 (0.48;1.90)</td>
</tr>
<tr>
<td>Burkhoff et al.</td>
<td>30 days</td>
<td>9/19</td>
<td>1.33 (0.57;3.10)</td>
</tr>
<tr>
<td>ISAR-SHOCK</td>
<td>30 days</td>
<td>6/13</td>
<td>1.00 (0.44;2.29)</td>
</tr>
<tr>
<td>IMPRESS in Severe Shock</td>
<td>30 days</td>
<td>11/24</td>
<td>0.92 (0.51;1.66)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>35/77</td>
<td>1.01 (0.70;1.44)</td>
</tr>
</tbody>
</table>
Inotrope Harm in Cardiogenic Shock

1. Marked increase in $\text{MVO}_2$ at a time of oxygen starvation.
2. Tachycardia increases $\text{MVO}_2$ and decreases diastolic interval.
3. Marked increase in LVEDP causes further decrease in diastolic perfusion pressure and increased wall tension.
4. Tachycardia mediated apoptosis may decrease myocardial recovery.
Increased Inotrope Exposure is associated with Mortality in AMI/CGS

Mortality and Number of Inotropes from cVAD Registry¹

\[ P<0.001 \text{ (N=287)} \]

<table>
<thead>
<tr>
<th>Number of Inotropes/Pressors</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>32%</td>
</tr>
<tr>
<td>1</td>
<td>54%</td>
</tr>
<tr>
<td>2</td>
<td>65%</td>
</tr>
<tr>
<td>3</td>
<td>65%</td>
</tr>
<tr>
<td>4+</td>
<td>74%</td>
</tr>
</tbody>
</table>


Samuels LE et al., J Card Surg. 1999
SG USE ASSOCIATED WITH IMPROVED OUTCOMES

Distribution of Survival to Explant at Impella Sites
(379 sites supported >4 AMICS patients)

Survival
0% to 10%
10% to 20%
20% to 30%
30% to 40%
40% to 50%
50% to 60%
60% to 70%
70% to 80%
80% to 90%
90% to 100%

Total # of Patients
N=68
N=147
N=277
N=488
N=777
N=465
N=425
N=331
N=99
N=62

ABIOMED INTERNAL CLINICAL QUALITY DATA
AMICS April 2015 – March 2016
Hemodynamic Monitoring associated with Improved Survival in AMI/CGS

IQ Database\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>No Hemodynamic Monitoring</th>
<th>Hemodynamic Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>49%</td>
<td>63%</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.0001</td>
<td>0.002</td>
</tr>
<tr>
<td>N=8767</td>
<td>N=5217</td>
<td></td>
</tr>
</tbody>
</table>

cVAD Registry\(^2\)

<table>
<thead>
<tr>
<th></th>
<th>No Hemodynamic Monitoring</th>
<th>Hemodynamic Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>68%</td>
<td>76%</td>
</tr>
<tr>
<td>P</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>N=634</td>
<td>N=516</td>
<td></td>
</tr>
</tbody>
</table>

2. cVAD survival to explant 2009-2016
Key Issues

• Culprit-Shock
• Cardiac Arrest-Cardiogenic shock interaction
• New AHA Scientific Statement-Shock centers and Shock teams
• Refractory Shock
PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock

Multivessel PCI in Cardiogenic Shock

Metaanalysis Mortality – Registry-Data:
10 observational studies published between 2003 and 2016

6,051 patients:
IABP-SHOCK II, ALKK, KAMIR, Yang et al., Cavender et al.; Mylotte et al., van der Schaaf et al., EHS-PCI, NCDR, SHOCK

- Culprit only-PCI (n=4,857)
- Multivessel-PCI (n=1,194)
Multivessel PCI in Cardiogenic Shock?
Metaanalysis Mortality – Registry-Data

<table>
<thead>
<tr>
<th></th>
<th>MV-PCI</th>
<th></th>
<th>C-PCI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>IABP-SHOCK II</td>
<td>75</td>
<td>167</td>
<td>119</td>
<td>284</td>
</tr>
<tr>
<td>ALKK</td>
<td>81</td>
<td>173</td>
<td>201</td>
<td>562</td>
</tr>
<tr>
<td>KAMIR</td>
<td>13</td>
<td>124</td>
<td>56</td>
<td>386</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>19</td>
<td>60</td>
<td>68</td>
<td>278</td>
</tr>
<tr>
<td>Cavender et al.</td>
<td>20</td>
<td>43</td>
<td>42</td>
<td>156</td>
</tr>
<tr>
<td>EHS-PCI</td>
<td>40</td>
<td>82</td>
<td>95</td>
<td>254</td>
</tr>
<tr>
<td>NCDR</td>
<td>158</td>
<td>433</td>
<td>737</td>
<td>2654</td>
</tr>
<tr>
<td>Overall</td>
<td>406</td>
<td>1082</td>
<td>1318</td>
<td>4574</td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2=0.007, P=31.0\%, p=0.19$
Test for overall effect: $p=0.001$

<table>
<thead>
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<th>C-PCI</th>
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<tr>
<td></td>
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</tr>
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<td>167</td>
<td>149</td>
<td>284</td>
</tr>
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<td>16</td>
<td>124</td>
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<td>386</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>21</td>
<td>60</td>
<td>85</td>
<td>278</td>
</tr>
<tr>
<td>Cavender et al.</td>
<td>32</td>
<td>43</td>
<td>101</td>
<td>156</td>
</tr>
<tr>
<td>Mylotte et al.</td>
<td>37</td>
<td>66</td>
<td>82</td>
<td>103</td>
</tr>
<tr>
<td>van der Schaaf et al.</td>
<td>22</td>
<td>37</td>
<td>66</td>
<td>124</td>
</tr>
<tr>
<td>SHOCK</td>
<td>7</td>
<td>9</td>
<td>26</td>
<td>57</td>
</tr>
<tr>
<td>Overall</td>
<td>226</td>
<td>506</td>
<td>578</td>
<td>1387</td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2=0.043, P=67.8\%, p=0.005$
Test for overall effect: $p=0.77$
Hypothesis

Culprit lesion only PCI (with possible staged revascularization) is superior to immediate multivessel PCI in multivessel coronary artery disease (≥2 mm in diameter, >70% stenosis incl. CTO) patients with cardiogenic shock complicating acute myocardial infarction.
Statistical Methodology

Primary Study Endpoint:
- 30-day all-cause mortality or renal replacement therapy

Secondary Study Endpoints:
- 30-day all-cause mortality
- Renal failure with requirement of renal replacement therapy
- Time to hemodynamic stabilization
- Duration of catecholamine therapy
- Serial creatinine-clearance
- Length of ICU-stay
- SAPS-II score
- Requirement and length of mechanical ventilation
- All-cause death within 6 and 12 months follow-up
- Recurrent infarction within 30-days, 6 and 12 months follow-up
- Death or recurrent infarction at 6 and 12 months follow-up
- Rehospitalization for congestive heart failure within 30 days, 6-, and 12-months follow-up
- Death/recurrent infarction/rehospitalization for congestive heart failure within 30 days, 6-, and 12-months follow-up
- Need for repeat revascularization (PCI and/or CABG) within 30 days, 6-, and 12-months follow-up
- Peak creatine kinase, creatine kinase-MB and troponin level during hospital stay

Sample Size:
- Estimated 50% event rate in multivessel PCI versus 38% in culprit lesion only group for primary endpoint
- 1 interim analysis (50% of patients)
- 2-sided Chi²-test; power: 80%, alpha=0.048 for final analysis → 684 patients
- To compensate losses in follow-up → 706 patients
1075 patients with acute myocardial infarction (STEMI and NSTEMI) and cardiogenic shock screened

369 excluded

706 randomized

355 randomized to immediate multivessel PCI

342 full informed consent

344 full informed consent

351 randomized to culprit lesion only PCI

301 culprit lesion only PCI

43 immediate multivessel PCI

60 staged PCI

1 staged CABG

13 urgent PCI

310 immediate multivessel PCI

310 immediate multivessel PCI

32 culprit lesion only PCI

8 staged PCI

0 staged CABG

5 urgent PCI

8 staged PCI

344 with 30-day follow-up

341 with 30-day follow-up

1 lost to follow-up

344 primary endpoint analysis

341 primary endpoint analysis

341 primary endpoint analysis
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Culprit only PCI (n=344)</th>
<th>Multivessel PCI (n=342)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years); median (IQR)</td>
<td>70 (60-78)</td>
<td>70 (60-77)</td>
</tr>
<tr>
<td>Male sex; n/total (%)</td>
<td>257/343 (74.9)</td>
<td>267/342 (78.1)</td>
</tr>
<tr>
<td>Prior myocardial infarction; n/total (%)</td>
<td>60/339 (17.7)</td>
<td>53/335 (15.8)</td>
</tr>
<tr>
<td>Prior PCI; n/total (%)</td>
<td>64/339 (18.9)</td>
<td>63/335 (18.8)</td>
</tr>
<tr>
<td>Prior coronary arterial bypass surgery; n/total (%)</td>
<td>20/341 (5.9)</td>
<td>13/337 (3.9)</td>
</tr>
<tr>
<td>Signs of impaired organ perfusion; n/total (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>237/341 (69.5)</td>
<td>224/341 (65.7)</td>
</tr>
<tr>
<td>Cold, clammy skin and extremities</td>
<td>233/338 (68.9)</td>
<td>236/335 (70.4)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>80/334 (24.0)</td>
<td>93/326 (28.5)</td>
</tr>
<tr>
<td>Arterial lactate &gt;2.0 mmol/l</td>
<td>216/334 (64.7)</td>
<td>224/330 (67.9)</td>
</tr>
<tr>
<td>Fibrinolysis &lt;24 h before randomization; n/total (%)</td>
<td>19/341 (5.6)</td>
<td>15/341 (4.4)</td>
</tr>
<tr>
<td>Resuscitation before randomization; n/total (%)</td>
<td>177/341 (51.9)</td>
<td>189/342 (55.3)</td>
</tr>
<tr>
<td>ST-elevation myocardial infarction; n/total (%)</td>
<td>206/335 (61.5)</td>
<td>209/330 (63.3)</td>
</tr>
<tr>
<td>No. of diseased vessels; n/total (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3/343 (0.9)</td>
<td>2/342 (0.6)</td>
</tr>
<tr>
<td>2</td>
<td>122/343 (35.6)</td>
<td>124/342 (36.3)</td>
</tr>
<tr>
<td>3</td>
<td>218/343 (63.6)</td>
<td>216/342 (63.2)</td>
</tr>
<tr>
<td>Patients with at least one CTO; n/total (%)</td>
<td>77/344 (22.4)</td>
<td>82/342 (24.0)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%); median (IQR)</td>
<td>33 (25-40)</td>
<td>30 (21-40)</td>
</tr>
</tbody>
</table>
## Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Culprit only PCI (n=344)</th>
<th>Multivessel PCI (n=342)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral access; n/total (%)</td>
<td>287/343 (83.7)</td>
<td>277/342 (81.0)</td>
<td>0.36</td>
</tr>
<tr>
<td>Radial access; n/total (%)</td>
<td>61/343 (17.8)</td>
<td>66/342 (19.3)</td>
<td>0.61</td>
</tr>
<tr>
<td>Stent implanted in culprit lesion; n/total (%)</td>
<td>326/343 (95.0)</td>
<td>324/342 (94.7)</td>
<td>0.86</td>
</tr>
<tr>
<td>Drug-eluting stent in culprit lesion; n/total (%)</td>
<td>305/326 (93.6)</td>
<td>308/324 (95.1)</td>
<td>0.41</td>
</tr>
<tr>
<td>TIMI flow III post PCI of culprit lesion; n/total (%)</td>
<td>289/342 (84.5)</td>
<td>293/338 (86.7)</td>
<td>0.46</td>
</tr>
<tr>
<td>Immediate PCI of non-culprit lesions; n/total (%)</td>
<td>43/344 (12.5)</td>
<td>310/342 (90.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Immediate complete revascularization; n/total (%)</td>
<td>26/344 (7.6)</td>
<td>277/342 (81.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total amount of contrast agent (ml); median (IQR)</td>
<td>190 (140-250)</td>
<td>250 (200-350)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Staged PCI of non-culprit lesions; n/total (%)</td>
<td>60/344 (17.4)</td>
<td>8/341 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Staged coronary artery bypass surgery; n/total (%)</td>
<td>1/344 (0.3)</td>
<td>0/341</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Mechanical circulatory support; n/total (%)</td>
<td>99/344 (28.8)</td>
<td>95/342 (27.8)</td>
<td>0.77</td>
</tr>
<tr>
<td>Intraaortic balloon pump; n/total (%)</td>
<td>25/99 (25.3)</td>
<td>26/95 (27.4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Impella 2.5; n/total (%)</td>
<td>16/99 (16.2)</td>
<td>18/95 (18.9)</td>
<td>0.61</td>
</tr>
<tr>
<td>Impella CP; n/total (%)</td>
<td>30/99 (30.3)</td>
<td>18/95 (18.9)</td>
<td>0.07</td>
</tr>
<tr>
<td>TandemHeart; n/total (%)</td>
<td>2/99 (2.0)</td>
<td>0/95</td>
<td>0.50</td>
</tr>
<tr>
<td>ECMO; n/total (%)</td>
<td>18/99 (18.2)</td>
<td>27/95 (28.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Mild hypothermia; n/total (%)</td>
<td>111/344 (32.3)</td>
<td>118/340 (34.7)</td>
<td>0.50</td>
</tr>
<tr>
<td>Mechanical ventilation; n/total (%)</td>
<td>273/344 (79.4)</td>
<td>282/339 (83.2)</td>
<td>0.20</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (days); median (IQR)</td>
<td>3 (1-7)</td>
<td>3 (1-7)</td>
<td>0.97</td>
</tr>
<tr>
<td>Duration of intensive care treatment (days); median (IQR)</td>
<td>5 (2-12)</td>
<td>5 (2-11)</td>
<td>0.61</td>
</tr>
</tbody>
</table>
Primary Study Endpoint
All-Cause Mortality or Renal Replacement Therapy

Relative risk 0.83; 95% confidence interval 0.71-0.96; P=0.01

Number at risk:
Culprit lesion only PCI 344
Immediate multivessel PCI 341

Days after randomization

All-cause mortality or renal replacement therapy (%)

0 5 10 15 20 25 30 35 40 45 50 55 60

Immediate multivessel PCI 55.4%
Culprit lesion only PCI 45.9%
All-Cause Mortality

Relative risk 0.84; 95% confidence interval 0.72-0.98; P=0.03

Number at risk:
Culprit lesion only PCI 344
Immediate multivessel PCI 341

Culprit lesion only PCI
Immediate multivessel PCI

51.5% 43.3%
Renal Replacement Therapy

Relative risk 0.71; 95% confidence interval 0.49-1.03; P=0.07

Number at risk:
Culprit lesion only PCI 344
Immediate multivessel PCI 341

Days after randomization

Renal replacement therapy (%)
Arterial Lactate

*No adjustment for multiple testing
Glomerular Filtration Rate

- Baseline: P=0.87*
- Day 1: P=0.56*
- Day 2: P=0.12*
- Day 3: P=0.04*
- Day 4: P=0.04*

*No adjustment for multiple testing

Estimated glomerular filtration rate (ml/min)

- **Blue diamond**: Culprit lesion only PCI
- **Red diamond**: Immediate multivessel PCI

**Legend:**
- Culprit lesion only PCI
- Immediate multivessel PCI
Conclusions

- In patients with multivessel coronary artery disease and cardiogenic shock complicating acute myocardial infarction culprit lesion only PCI with possible staged revascularization reduced the composite of mortality or requirement for renal replacement therapy at 30 days.

- This effect in the primary outcome was mainly driven by a 30-day mortality reduction.

- This largest randomized European multicenter trial in cardiogenic shock complicating myocardial infarction challenges current guideline recommendations.
Key Issues

- Culprit-Shock
- Cardiac Arrest-Cardiogenic shock interaction
- New AHA Scientific Statement-Shock centers and Shock teams
- Refractory Shock
Cardiac Arrest

- Out-of-hospital cardiac arrest (OOHCA)
- 295,000 people annually in the US
- 7.9% median survival rate
- Anoxic encephalopathy and neurologic deficits
- Therapeutic hypothermia (TH) clinical trials
- ILCOR recommendation for TH after resuscitation

# Interaction of Cardiac Arrest and Cardiogenic Shock

<table>
<thead>
<tr>
<th>Cardiac Arrest</th>
<th>Cardiogenic Shock (+)</th>
<th>Cardiogenic Shock (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>184 Patients</td>
<td>In-hospital Mortality: 47.3%</td>
<td>317 Patients In-hospital Mortality: 20.2%</td>
</tr>
<tr>
<td>1 – Year Mortality: 51.6%</td>
<td>1 – Year Mortality: 22.7%</td>
<td></td>
</tr>
<tr>
<td>259 Patients</td>
<td>In-hospital Mortality: 25.1%</td>
<td>4157 Patients In-hospital Mortality: 1.7%</td>
</tr>
<tr>
<td>1 – Year Mortality: 33.6%</td>
<td>1 – Year Mortality: 5.5%</td>
<td></td>
</tr>
</tbody>
</table>
OHCA survival to hospital discharge by 5-year time periods

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Pooled Survival Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(95% Confidence Interval)</td>
</tr>
<tr>
<td>1980-1984</td>
<td>8.1 (0.9, 15.3)</td>
</tr>
<tr>
<td>1985-1989</td>
<td>3.3 (1.9, 4.7)</td>
</tr>
<tr>
<td>1990-1994</td>
<td>9.5 (7.4, 11.6)</td>
</tr>
<tr>
<td>1995-1999</td>
<td>7.4 (5.6, 9.0)</td>
</tr>
<tr>
<td>2000-2004</td>
<td>6.2 (4.8, 7.6)</td>
</tr>
<tr>
<td>2005-2008</td>
<td>7.8 (6.1, 9.5)</td>
</tr>
<tr>
<td>Overall</td>
<td>7.6 (6.7, 8.4)</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
Survival improves to 50-60% with Favorable neurological outcomes in 86% of survivors

Rab et al. JACC 2015;66:62-73

**TABLE 1** 28 Clinical Reports of Combining TTM and Early Coronary Angiography in Resuscitated, But Comatose Patients With STEMI on the ECG

<table>
<thead>
<tr>
<th>First Author, Date (Ref. #)</th>
<th>Survivors to DC (n = 2,687/4,510 [60%])</th>
<th>Good Neuro Among Survivors (n = 2,090/2,426 [86%])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hovdenes et al., 2007 (17)</td>
<td>41/50</td>
<td>34/41</td>
</tr>
<tr>
<td>Richling et al., 2007 (33)</td>
<td>24/46</td>
<td>22/24</td>
</tr>
<tr>
<td>Knafelj et al., 2007 (18)</td>
<td>30/40</td>
<td>22/30</td>
</tr>
<tr>
<td>Wolfrum et al., 2008 (22)</td>
<td>12/16</td>
<td>11/12</td>
</tr>
<tr>
<td>Peels et al., 2008 (104)</td>
<td>22/44</td>
<td>NA</td>
</tr>
<tr>
<td>Schefold et al., 2009 (34)</td>
<td>NA</td>
<td>19/31</td>
</tr>
<tr>
<td>Reynolds et al., 2009 (14)</td>
<td>52/96</td>
<td>NA</td>
</tr>
<tr>
<td>Nielsen et al., 2009 (35)</td>
<td>303/479</td>
<td>278/303</td>
</tr>
<tr>
<td>Batista et al., 2010 (27)</td>
<td>8/20</td>
<td>6/8</td>
</tr>
<tr>
<td>Dumas et al., 2010 (3)</td>
<td>177/435</td>
<td>160/171</td>
</tr>
<tr>
<td>Koeth et al., 2010 (105)</td>
<td>114/143</td>
<td>NA</td>
</tr>
<tr>
<td>Stub et al., 2011 (28)</td>
<td>52/81</td>
<td>46/52</td>
</tr>
<tr>
<td>Laish-Farkash et al., 2011 (36)</td>
<td>69/110</td>
<td>59/69</td>
</tr>
<tr>
<td>Tamte et al., 2011 (37)</td>
<td>140/252</td>
<td>132/140</td>
</tr>
<tr>
<td>Radsel et al., 2011 (31)</td>
<td>154/212</td>
<td>128/154</td>
</tr>
<tr>
<td>Mooney et al., 2011 (12)</td>
<td>78/140</td>
<td>72/78</td>
</tr>
<tr>
<td>Cronier et al., 2011 (11)</td>
<td>60/111</td>
<td>54/60</td>
</tr>
<tr>
<td>Gräsnér et al., 2011 (90)</td>
<td>143/183</td>
<td>118/143</td>
</tr>
<tr>
<td>Bro-Jeppesen et al., 2012 (30)</td>
<td>211/360</td>
<td>207/219</td>
</tr>
<tr>
<td>Zanuttini et al., 2012 (10)</td>
<td>29/48</td>
<td>NA</td>
</tr>
<tr>
<td>Liu et al., 2012 (106)</td>
<td>36/81</td>
<td>NA</td>
</tr>
<tr>
<td>Nanjayya et al., 2012 (59)</td>
<td>18/35</td>
<td>14/18</td>
</tr>
<tr>
<td>Strote et al., 2012 (58)</td>
<td>44/61</td>
<td>34/44</td>
</tr>
<tr>
<td>Waldo et al., 2013 (107)</td>
<td>57/84</td>
<td>NA</td>
</tr>
<tr>
<td>Velders et al., 2013 (32)</td>
<td>187/222</td>
<td>168/183</td>
</tr>
<tr>
<td>Callaway et al., 2014 (43)</td>
<td>495/765</td>
<td>413/495</td>
</tr>
<tr>
<td>Thomas et al., 2014 (108)</td>
<td>168/348</td>
<td>115/168</td>
</tr>
<tr>
<td>Sideris et al., 2014 (88)</td>
<td>97/300</td>
<td>80/97</td>
</tr>
</tbody>
</table>

Values are n/N.
DC = discharge; ECG = electrocardiogram; neuro = neurological function; TTM = targeted temperature management.
Early predictors of survival in OHCA

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>[95% Conf.Interval]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time From BLS to ROSC ≥ 15 minutes</td>
<td>0.28</td>
<td>(0.19-0.55)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time From Collapse to BLS &gt; 5 minutes</td>
<td>0.32</td>
<td>(0.17-0.49)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diabete mellitus</td>
<td>0.42</td>
<td>(0.20-0.84)</td>
<td>0.015</td>
</tr>
<tr>
<td>Age &gt; 59yrs</td>
<td>0.45</td>
<td>(0.27-0.75)</td>
<td>0.002</td>
</tr>
<tr>
<td>Initial Arrest Rhythm: Asystole/PEA</td>
<td>0.51</td>
<td>(0.30-0.88)</td>
<td>0.035</td>
</tr>
<tr>
<td>Blood lactate (for each quartile increase )</td>
<td>0.55</td>
<td>(0.44-0.70)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ST segment elevation</td>
<td>1.09</td>
<td>(0.60-1.98)</td>
<td>0.778</td>
</tr>
<tr>
<td>Successfull PCI</td>
<td>2.06</td>
<td>(1.16-3.66)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Out-of-hospital cardiac arrest (OHCA) patients who have achieved return of spontaneous circulation (ROSC), but remain comatose

Within 10 minutes of hospital arrival:
- Perform 12-lead electrocardiography (ECG) to identify patients who benefit from emergent angiography
- Induce targeted temperature management (TTM) with mild therapeutic hypothermia (TH) to limit tissue injury following cardiac arrest

ST-segment elevation on the ECG

Activate ST-segment elevation myocardial infarction (STEMI) team
- Consider survival benefit/risk ratio, especially if multiple unfavorable resuscitation features are present

No ST-segment elevation on the ECG

“ACT”
- Assess for unfavorable resuscitation features
- Consult with interventional cardiology & intensive care services
- Transport to cardiac catheterization laboratory (CCL) (once a decision is made to proceed with coronary angiography)

Patients deemed suitable
- Emergency angiography
- Define coronary anatomy
- Identify coronary lesion
- Percutaneous coronary intervention (PCI)
- Left ventricular (LV) function and hemodynamic assessment
- Provide mechanical LV support if needed

Patients with multiple unfavorable resuscitation features
- Unwitnessed arrest
- Initial rhythm: Non-VF
- No bystander CPR
- >30 min to ROSC
- Ongoing CPR
- pH <7.2
- Lactate >7
- Age >85
- End stage renal disease
- Noncardiac causes (e.g., traumatic arrest)

Patients are less likely to benefit from coronary intervention
- Individualized patient care and interventional cardiology consultation are strongly recommended

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Key Issues

- Culprit-Shock
- Cardiac Arrest-Cardiogenic shock interaction
- New AHA Scientific Statement-Shock centers and Shock teams
- Refractory Shock
Contemporary Management of Cardiogenic Shock
A Scientific Statement From the American Heart Association

Abstract: Cardiogenic shock is a high-acuity, potentially complex, and hemodynamically diverse state of end-organ hypoperfusion that is frequently associated with multisystem organ failure. Despite improving survival in recent years, patient morbidity and mortality remain high, and there are few evidence-based therapeutic interventions known to clearly improve patient outcomes. This scientific statement on cardiogenic shock summarizes the epidemiology, pathophysiology, causes, and outcomes of cardiogenic shock; reviews contemporary best medical, surgical, mechanical circulatory support, and palliative care practices; advocates for the development of regionalized systems of care; and outlines future research priorities.

Cardiogenic shock (CS) is a low-cardiac-output state resulting in life-threatening end-organ hypoperfusion and hypoxia. Acute myocardial infarction (MI) with left ventricular (LV) dysfunction remains the most frequent cause of CS. Advances in reperfusion therapy have been associated with improvements in survival, but significant regional disparities in evidence-based care have been reported, and in-hospital mortality remains high (27%–51%). Management recommendations are distributed between disease-specific statements and guidelines, and a dedicated and comprehensive clinical resource in this area is lacking. Thus, consolidating the evidence to define contemporary best medical and surgical CS practice for both MI-associated CS and other types of CS may be an important step in knowledge translation to help attenuate disparities in evidence-based care.

Regional systems of care coupled with treatment algorithms have improved survival in high-acuity time-sensitive conditions such as MI, out-of-hospital cardiac arrest (OHCA), and trauma. Applying a similar framework to CS management may lead to similar improvements in survival, and CS systems of care are emerging within existing regional cardiovascular emergency care networks; however, guidance from a national expert group on structure and systems of care has not been available. According to the purposes of this American Heart Association (AHA) scientific statement on CS to summarize our contemporary understanding of the epidemiology, pathophysiology, and in-hospital best care practices into a single clinical resource document; to suggest a stepwise management algorithm that integrates medical, surgical, and mechanical circulatory support (MCS) therapies; and to propose a Mission: Lifesaving-supported pathway for the development of integrated regionalized CS systems of care.

Key Words: AHA Scientific Statement | Delivery of health care | Disease management | Shock, cardiogenic

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Detroit Cardiogenic Shock Initiative

DETROIT
CSI
Detroit CSI Protocol

1. RAPID Identification of Cardiogenic Shock
   - Cath Lab Activation
   - Obtain Femoral Access
   - LVEDP
     - < 15 mmHg: Consider Other Causes of Shock
     - ≥ 15 mmHg: IMPELLA

Door To Support Time
Target: < 90 minutes
# Detroit CSI Protocol

1. **Impella Support**
   - **PCI**
   - **Right Heart Cath**

   - **CPO < 0.6**
     - PAPI < 0.9
       - Possible RV Failure
         - Consider RV Support
     - PAPI > 0.9
       - RV Normal

   - **CPO ≥ 0.6 and PAPI > 0.9**
     - Continue to Titrate
       - Pressors/Inotropes

2. Consider ↑ of LV Support or Transfer to LVAD Center
**Detroit CSI Protocol**

1. **Admission to ICU/CCU**
2. **12 Hours Post-Impella**
   - CPO / PAPI / Lactate
3. **Titrates ↓ Pressors/Inotropes**
4. **24 Hours Post-Impella**
   - CPO / PAPI / Lactate

   - **CPO < 0.6**
     - Consider ↑ of Mechanical Support
   - **CPO ≥ 0.6**
     - Continue to ↓ Titrates or D/C Pressors/Inotropes
Physicians from over 40 hospitals have contacted us about joining Detroit CSI

First site outside of Detroit launched in August:

- Mercy Fitzgerald Hospital in Philadelphia

Similar to Detroit, regional groups are forming to work together on CGS

Detroit Cardiogenic Shock Initiative
National Outcomes Improving

Distribution of Impella Site Outcomes

Survival to Explant

22% relative improvement in overall outcomes since March, 2016 (p<0.0001)

2. 525 sites supporting >6 AMICS patients, 7,483 patients total since March 2016
Key Issues

- Culprit-Shock
- Cardiac Arrest-Cardiogenic shock interaction
- New AHA Scientific Statement-Shock centers and Shock teams
- Refractory Shock
Early Transport to Cath Lab for ECMO and Revasc in Refractory VF (OHCA)

CENTRAL ILLUSTRATION: Refractory Cardiac Arrest Due to VF/VT and the University of Minnesota ECLS/PCI Protocol

Early Transport to Cath Lab for ECMO and Revascularization in Refractory Ventricular Fibrillation

**Out of Hospital**
- VF/VT Initial rhythm
- DCCV x3 and 300mg Amiodarone without ROSC
- Time to CCL <30 min

**Initial CCL**
- ABG and lactate
- Stop if: ETCO2<10mmHg, PaO2<50mmHg or Lactate >18 mmol/L
- If ROSC, immediate Cor Angio +/- IABP.
- If no ROSC, ECLS, then Cor Angio +/- IABP.
- Continue ACLS/ECLS for 90 minutes/PCI; if no ROSC by 90 minutes, declared dead
72 Patients Transported by EMS (Admitted to CCL)

10/72 (14%) Excluded Not Meeting Early EMS Transport Criteria
- 3 - Manual CPR Only
- 1 - Pectus Excavatum
- 2 - Morbid Obesity
- 3 - Time from 911 Call to CCL > 90 minutes
- 1 - Age > 80 years; terminal cancer
- 1 - Stage IV renal cell cancer
- 2 - DNR discovered on CCL arrival

62/72 (86%) Patients Met Early EMS Transport Criteria (Study Population)

7/62 (11%) met CCL Discontinuation of Resuscitation Criteria and Declared Dead

55/62 (89%) Patients had Continued CCL Resuscitation and Received Coronary Angiography
- 5/55 (9%) had ROSC Prior to CCL Arrival
- 50/55 (91%) placed on ECLS prior to coronary angiography
- 46/55 (84%) patients received PCI

8/50 (16%) ECLS Patients Declared Dead in CCL Due to Failure to Achieve Sustained Organized Electrical Rhythm after 90 Minutes

47/62 (76%) Patients Admitted to the Hospital (CICU)
Comparison Between the Refractory VF/VT Protocol and the Historical

- All Patients: n = 170 (Historical) vs n = 62 (Protocol)
- ROSC on ED Arrival: n = 63 (Historical) vs n = 5 (Protocol)
- Hospital Admission: n = 51 (Historical) vs n = 47 (Protocol)
- Hospital DC: n = 30 (Historical) vs n = 28 (Protocol)
- DC with CPC 1&2: n = 26 (Historical) vs n = 26 (Protocol)
Level One Shock Team: Early Experience in ECMO use as a Rescue Device in Cardiac Arrest from ST-Elevation Myocardial Infarction in the Cardiac Catheterization Laboratory

Michael Mooney, David Hildebrandt, David Feldman, Benjamin Sun, Dirck Rilla, Yale Wang, Ivan Chavez, M. Nicholas Burke, Timothy Henry, Minneapolis Heart Institute, Minneapolis, MN

Background
- Patients who present with ST-Elevation Myocardial Infarction (STEMI) complicated by cardiogenic shock (CS) that suffer a cardiac arrest have high mortality rates
- Little data exist on using Extracorporeal Membrane Oxygenation (ECMO) as a rescue device during CPR in the CS patient

Methods
- We reviewed all patients from 8/2011 to 10/2012 who presented to a high volume, tertiary percutaneous coronary intervention (PCI) center with STEMI complicated by CS that developed a PEAK arrest during PCI and remained hemodynamically unstable despite mechanical CPR, IABP and inotropes
- Patients were placed on percutaneous antero-venous ECMO as a rescue device, were intubated, and were found to be hypoperfused with profound metabolic acidosis
- Mechanical CPR via the LUCAS device was used on all patients
- Antegrade perfusion was established below the arterial ECMO sheath in all cases

Results
- The five patients included 2 males and 3 females with a median age of 64
- Median time of arrest to initiation of ECMO was 52 minutes (Range 16-132)
- ECMO was required for a median time of 4 days (Range 3-6)
- Therapeutic Hypothermia (TH) was instituted after initiation of ECMO in 4 (80%) cases
- EF’s of < 10% were noted in 4 cases and 1 patient had no cardiac output present prior to initiation of ECMO
- Four out of five patients (80%) survived to hospital discharge
- All of the survivors had good neurocognitive recovery (CPC score of 1 or 2) at discharge
- Of four survivors, discharge EF improved to a median of 46% (25-68%)
- Bleeding, which required transfusion occurred in all cases

Figure
- Figure 1. Emergency “E-ECMO” Multidisciplinary, experienced team members that rapidly respond and come together when a patient is emergently placed on ECMO.

Conclusions
- ECMO can be a life saving technique when instituted by an experienced Shock Team in the CVLaboratory for refractory PEAK occurring in the CV lab
- LUCAS CPR was a valuable adjunct
- Striking recovery of LV function can also occur in several days
- The combination of ECMO and TH was associated with excellent neurological outcomes as well
- Recovery was not expected, but did occur despite lack of Left Ventricular unloading
- ECMO may have a role in selected PCI centers with advanced specialized teams
Complication Rate

- 13% on ECMO had Vascular Complications
- 4 with significant retroperitoneal bleeding requiring transfusion
- 3 developed an ischemic leg after thrombosis of the distal perfusion cath
“Oh, Lord! Here come circumstances beyond our control.”