Module 1: The Critical Science: Understanding the ABCs of Mechanical Circulatory Support

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Disclosure

All presenters have a speaker agreement with Maquet

Disclaimer – Indications

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Goals of Mechanical Circulatory Support
A: Myocardial Protection

**DEMAND**
- Heart Rate
- Contractility
- Afterload

**SUPPLY**
- Diastolic Pressure (DPTI)
- Microvascular resistance
- Coronary Patency
B: Organ Perfusion

- **Tissue blood flow**
  - \( F = \frac{MAP}{VR} \)
  - **Local vascular resistance**
  - **Mean aortic pressure**
    - \( MAP = CO \times TPR \)

- **Cardiac output**
  - \( CO = HR \times SV \)

- **Stroke volume**
  - \( SV = EDV - ESV \)
  - **Heart rate**
  - **Total peripheral resistance**

- **End-diastolic volume**
  - **End-systolic volume**

- **Afterload**
  - **Contractility**

**Filling pressure**

**Cardiac compliance**
C: Safety and Ease of Use

Bleeding
Vascular Complications
Cerebrovascular Complications

Availability
Rapid Initiation
Familiarity/Specialist Expertise
Circulatory Support Strategies
1. Inotropic Drugs
# 1. Inotropic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
<th>CO</th>
<th>SVR</th>
<th>MAP</th>
<th>Tissue VR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>DA β1 β2 agonism</td>
<td>↑↑</td>
<td>↓</td>
<td>↑↓</td>
<td>↓↑</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>A1 β 1/2 agonism</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>α1  β1 / 2 agonism</td>
<td>↑↓</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>Levosimendan</td>
<td>Ca++ sensitiser</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↑↓</td>
<td>↓</td>
</tr>
<tr>
<td>Milrinone</td>
<td>PDE inhibitor</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↑↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

Increased MVO$_2$
Increased tissue vascular resistance
2. Intra Aortic Balloon Pump
2. Intra Aortic Balloon Pump

![Graph showing pressure dynamics with arrows indicating unassisted systolic pressure, diastolic augmentation, assisted systolic pressure, and unassisted end diastolic pressure.]
2. Intra Aortic Balloon Pump

Coronary and Microvascular Physiology During Intra-Aortic Balloon Counterpulsation

JACC CV Interv, April 2014

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A Myocardial protection by improving myocardial perfusion and reducing oxygen demand, especially when Autoregulation is dysfunctional or exhausted

- Persistent ischemia (no reflow)
- Sustained hypotension
- Critical coronary disease (local maximal microvascular dilation)

B No direct effect on tissue perfusion (indirect effect via myocardial protection)

C Safe and Easy to use
# Intra-aortic Balloon Pump Trials: Questions, Answers and Unresolved Issues

## Table: Randomized Control Trials of Intra-aortic Balloon Counterpulsation

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Trial</th>
<th>n</th>
<th>Inclusion</th>
<th>Principal End Point</th>
<th>Results (IABP vs Control Group)</th>
<th>Timing of IABP Insertion</th>
<th>Crossover From Control to IABP Group, %</th>
<th>Bleeding Rates</th>
<th>Vascular Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk PCI (excluding shock/AMI)</td>
<td>Perera et al⁹</td>
<td>301</td>
<td>LVEF&lt;30% BCIS Jeopardy score&lt;8</td>
<td>Composite of death, AMI, CVA or further revascularization at hospital discharge (capped at 28 days)</td>
<td>15.2% vs 16%; OR, 0.94; 95% CI, 0.51-1.76; P=0.85</td>
<td>Pre-PCI 12.0</td>
<td>19.2% vs 11.3%; OR, 1.88; 95% CI, 0.93-3.79; P=0.06</td>
<td>3.3% vs 0%;  P=0.06 (at hospital discharge, capped at 28 days)</td>
<td></td>
</tr>
<tr>
<td>AMI-without shock</td>
<td>Perera et al¹⁰</td>
<td>182</td>
<td>All-cause mortality at follow-up (median 51 mo)</td>
<td></td>
<td>27.8% vs. 38.7%, HR 0.66; 95% CI, 0.44-0.98; P=0.039</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI complicated by cardiogenic shock</td>
<td>Ohman et al¹¹</td>
<td>437</td>
<td>STE-ACS or NSTEMI or urgent catheterization revealing an occluded vessel with regional LV dysfunction</td>
<td>Recurrence of infarct-related artery &amp; reocclusion, stroke, new-onset heart failure, or sustained hypotension</td>
<td>28.9% vs 29.2%;  P=0.95</td>
<td>Post-PCI 11.5</td>
<td>36% vs 27%;  P=0.05</td>
<td>0.5% vs 0.4%;  P=1.0 (in-hospital; requiring surgical intervention)</td>
<td></td>
</tr>
<tr>
<td>AMI complicated by cardiogenic shock</td>
<td>van’t Hof et al¹²</td>
<td>238</td>
<td>STE-ACS Primary PCI</td>
<td>Composite of death, nonfatal reinfarction, stroke or EF&lt;30% at 6 mo</td>
<td>26% vs. 26%;  P=0.94</td>
<td>Post-PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI complicated by cardiogenic shock</td>
<td>Patel et al¹³</td>
<td>337</td>
<td>STE-ACS or NSTEMI Early PCI</td>
<td>Infarct size as a percentage of LV mass</td>
<td>42.1% vs 37.5%; P=0.07</td>
<td>Pre-PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI complicated by cardiogenic shock</td>
<td>Thiele et al¹⁰</td>
<td>600</td>
<td></td>
<td>30-d mortality</td>
<td>39.7% vs 41.3%; P=0.69</td>
<td>Operator discretion (86.6% after PCI)</td>
<td>3.3% vs 4.4%;  P=0.51 (severe life-threatening)</td>
<td>4.3% vs 3.4%;  P=0.53 (surgical vascular repair)</td>
<td></td>
</tr>
</tbody>
</table>

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3.1% vs 1.7%;  P=0.49 (at 30 days)  
4.3% vs 1.1%;  P=0.09 (at 30 days)  
3.3% vs 4.4%;  P=0.51 (severe life-threatening)  
4.3% vs 3.4%;  P=0.53 (surgical vascular repair)
3. Impella Recover

Direct LV Unloading by providing continuous (non-pulsatile)

LV -> aortic flow

2.5 L/min: 13F
3.5 L/min: 14F
5.0 L/min: 22F
3. Impella Recover

3. Impella Recover

**A:** Myocardial protection by decreasing afterload -> reducing oxygen demand (effects on myocardial perfusion??)

**B:** Improves cardiac output without increasing local vascular resistance -> improves tissue perfusion

**C:** (Relatively) Safe and Easy to use but increasing risk of vascular complications, especially with larger bore access

2.5 L/min: 13F
3.5 L/min: 14F
5.0 L/min: 22F
4. Extra-Corporeal Pumps

Tandem Heart
- LA -> Ao continuous flow
- Large bore arterial and venous access
- Trans-septal puncture

VA-ECMO/ECLS
- RA -> Ao continuous flow
- Large bore arterial and venous access
4. Extra-corporeal Pumps

- Improve cardiac output and tissue perfusion
  BUT at the cost of increased afterload -> increased MVO$_2$
  - (? Effect on coronary flow)
  - Vascular risk ++, Complexity ++
# Circulatory Support Strategies: Summary

<table>
<thead>
<tr>
<th></th>
<th>Myocardial Protection</th>
<th>Tissue Perfusion</th>
<th>Ease of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supply</td>
<td>Demand</td>
<td></td>
</tr>
<tr>
<td>Inotropic drugs</td>
<td>+/-</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ + + +</td>
</tr>
<tr>
<td>IABP</td>
<td>+ +</td>
<td>+</td>
<td>+ + +</td>
</tr>
<tr>
<td>Impella</td>
<td>?</td>
<td>+</td>
<td>+ +</td>
</tr>
<tr>
<td>VA-ECMO/ECLS</td>
<td>?</td>
<td>-</td>
<td>+ + + +</td>
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</table>

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>Desired effect</td>
</tr>
<tr>
<td>-</td>
<td>Undesirable effect</td>
</tr>
<tr>
<td>?</td>
<td>Missing/equivocal data</td>
</tr>
</tbody>
</table>
Selecting the right support strategy

Which device for which patient?

Characterise by Broad Diagnostic Category

OR

Individual Physiology?
**BCIS-1: Major Outcomes**

![Graph showing adverse events (%)](image)

Perera et al. JAMA 2010; 364(8):867-874

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**Primary outcome**

<table>
<thead>
<tr>
<th></th>
<th>All (N=337)</th>
<th>IABC (N=161)</th>
<th>SOC (N=176)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct size (% LV), modified ITT all patients with CMR data</td>
<td></td>
<td></td>
<td></td>
<td>0.060</td>
</tr>
<tr>
<td>N</td>
<td>275</td>
<td>133</td>
<td>142</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>39.8</td>
<td>42.1</td>
<td>37.5</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>38.8</td>
<td>42.8</td>
<td>36.2</td>
<td></td>
</tr>
<tr>
<td>Infarct size (% LV), modified ITT patients prox. LAD and TIMI flow 0/1</td>
<td></td>
<td></td>
<td></td>
<td>0.110</td>
</tr>
<tr>
<td>N</td>
<td>192</td>
<td>93</td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>44.4</td>
<td>46.7</td>
<td>42.3</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>42.1</td>
<td>45.1</td>
<td>38.6</td>
<td></td>
</tr>
<tr>
<td>Co-primary endpoint: 2-sided p=0.025</td>
<td>Patel et al. JAMA 2011;305(12):1329-37</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Primary Study Endpoint (30-Day Mortality)**

![Graph showing mortality (%) over time after randomization (Days)](image)

Thiele et al. NEJM 2012;367:1287-96

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**PROTECT II Interim Results**

![Table showing relative risk and group p-value](image)

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Impella</th>
<th>IABP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (N=100%)</td>
<td>38%</td>
<td>43%</td>
<td>0.40</td>
<td></td>
</tr>
</tbody>
</table>

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![Graph showing outcomes](image)
In Summary

• Principles and goals behind mechanical circulatory support
• Different support strategies and how they fit in with the principles
• Tailoring the support strategies for the individual patient