Intra-Aortic Balloon Pump (IABP) therapy: What does the evidence say?

NTI 2019
Class Code: EXED266
Intra-Aortic Balloon Pump (IABP) therapy: what does the evidence say?

Learning objectives

At the conclusion of this program, the participants will be able to:

1. Describe the spectrum of Mechanical Circulatory Support (MCS) options
2. Discuss the importance of considering MCS early in acute coronary syndrome, cardiac surgery and complications of heart failure patient’s clinical course
Intra-Aortic Balloon Pump (IABP) therapy: what does the evidence say?

- Treatment of cardiogenic shock (CS) is now routine in cardiac catheterization labs
- Research is challenged by the fact that the shock population is incredibly heterogeneous at presentation and throughout treatment
- Avoidance of multi-organ failure can affect treatment options
- Hemodynamic indices and laboratory values, such as lactate levels, can be accurate markers of clinical response to treatment
- Survival remains the ultimate measurable endpoint for CS

Intra-Aortic Balloon Pump (IABP) therapy: what does the evidence say?

• Standard treatment of CS consists primarily of volume management, inotropic agents and vasopressors
  - these treatments enhance tissue perfusion
• The hemodynamic benefits of inotropes and vasopressors are counterbalanced by adverse effects such as:
  - increased myocardial oxygen demand
  - arrhythmias
  - compromise of tissue microcirculation
• This can translate into an increased mortality risk
• MCS is a means to increase systemic blood flow
  - Avoid the possible cardiotoxicity and long-term morbidity of vasopressors

Treatment of cardiogenic shock
Escalation of MCS for left ventricular failure

- Early shock
  - No Inotrope: 2%
  - Low Dose: 3%
  - Moderate Dose: 8%
  - High Dose: 21%

- Refractory shock
  - Two High Dose: 42%
  - Three High Dose: 80%

Higher efficacy IAB + hemodynamic guided therapy

IABP/ECLS + antegrade catheter

In-Hospital Mortality

Support devices

- Despite early revascularization, CS mortality rates remain close to 50%
  - unchanged in over 20 years
- The demand for percutaneous MCS support has grown dramatically as the need has become more obvious.
- Theoretically, the best support option:
  - increases or maintains tissue perfusion
  - unloads the compromised ventricle
  - enhances coronary perfusion
  - easy to insert and use
  - low incidence of side effects
  - economical

Support devices

• For more than 30 years, the Intra-Aortic Balloon Pump (IABP) has been the sole option in most centers due to its.
  - bedside efficacy
  - ease of use
  - wide availability
  - clear safety profile

• New percutaneous ventricular assist devices (PVADs) have dramatically altered the landscape and broadened the scope of potential support options
### Physiologic principles of mechanical support

#### Comparison

<table>
<thead>
<tr>
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<th>IABP</th>
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<td><strong>Bleeding risk</strong></td>
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<td>+++</td>
<td>++</td>
<td>++</td>
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<tr>
<td><strong>Hemolysis risk</strong></td>
<td>0</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Limb ischemia Risk</strong></td>
<td>+</td>
<td>+++</td>
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</tbody>
</table>

Physiologic principles of mechanical support

IABP

- The mechanism of action of IABP is based on rapid inflation and deflation of a low-profile balloon catheter in the descending aorta during diastole
- The primary modes of effect are:
  - augmentation of diastolic blood pressure
  - increased coronary perfusion
  - reduction in afterload

Physiologic principles of mechanical support
IABP

Labeled indications include Acute Coronary Syndrome (ACS), cardiac and non-cardiac surgery, and complications of heart failure

• Examples of ACS and complications of heart failure umbrella include:
  - hemodynamic support during diagnostic or PCI procedures
  - complications of Myocardial Infarction (MI) including cardiogenic shock
  - Refractory unstable angina, impending infarction, post infarction angina or threatening extension of MI, ischemic related intractable ventricular arrhythmias


The original SHOCK trial (1999) provided a benchmark for outcomes from the early primary angioplasty era. In that study, 302 patients with acute MI and cardiogenic shock experienced a 50% mortality rate at 30 days.

- IABP use was recommended in the study protocol, and nearly 90% of all participants were treated with an IABP.

- Set a benchmark for mortality in cardiogenic shock that has not significantly changed over time;
  - **cardiogenic shock complicating acute MI has an approximate 50% short-term mortality**

Data supporting mechanical support during cardiogenic shock
IABP-SHOCK II study

- The 2012 IABP-SHOCK II study was well-conducted and remarkable in the field of cardiogenic shock for its relatively large size (600 patients) and rapid enrollment (completed in less than 3 years)
- Enrolled patients were critically ill as evidenced by their poor short-term survival

The primary endpoint of all-cause mortality at 30 days did not differ between the control or IABP arms (41% vs. 40%).

With the caveats associated with subgroup analysis, only treatment in younger patients (age <50 years) carried a signal for benefit with IABP.

Additional considerations in the study’s execution may have affected results:
- there was a 10% crossover rate with IABP usage in the control arm
- the timing of IABP insertion was left to the discretion of the operator
  - nearly 90% of patients had the IABP placed after PCI, and it is now accepted that early initiation of support may provide additional clinical benefit.

Data supporting mechanical support during cardiogenic shock

IABP-SHOCK II study

Comparative studies of IABP and PVADs

- A few small studies compare the IABP with novel percutaneous support devices
- These studies were all underpowered
- The results remain exploratory

<table>
<thead>
<tr>
<th>Study</th>
<th>IABP No. of patients</th>
<th>IABP Mortality</th>
<th>PVAD No. of patients</th>
<th>PVAD Mortality</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiele H, et al.¹¹</td>
<td>20</td>
<td>45%</td>
<td>21</td>
<td>43%</td>
<td>NS</td>
</tr>
<tr>
<td>ISAR-SHOCK¹²</td>
<td>13</td>
<td>46%</td>
<td>12</td>
<td>46%</td>
<td>NS</td>
</tr>
<tr>
<td>IMPRESS¹³</td>
<td>24</td>
<td>50%</td>
<td>24</td>
<td>50%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: IABP, intra-aortic balloon pump; NS, not significant; PVAD, percutaneous ventricular assist device.

Thiele and colleagues conducted a randomized study comparing IABP (n = 20) with TandemHeart (n = 21) in cardiogenic shock.

- Half of patients had suffered prior cardiac arrest, and nearly all were intubated.
- The primary aim was to quantify the hemodynamic effects of the novel system.
  - TandemHeart provided a greater improvement in cardiac output, pulmonary artery pressure, filling pressures and cardiac power index, though all parameters also improved in the IABP arm.

Comparative studies of IABP and PVADs

Thiele

- Despite the difference in device power, the use of inotropes was similar between groups
- Fever, bleeding, transfusion and coagulopathy were all more common with TandemHeart
- At 30 days, mortality was identical

Comparative studies of IABP and PVADs

ISAR-SHOCK

- Compared Impella 2.5 to IABP in a small cohort (n = 26) of shock patients
- Primary endpoint evaluating immediate hemodynamic changes
- Improvement in both groups’ parameters with a significantly greater immediate increase in cardiac index (0.49 vs. 0.11 L/min/m², P = .02) with Impella
- At 4 hours and 30 hours, cardiac index was identical for both groups
- Severity of illness scores and survival were similar
- Transfusion and hemolysis were more common with Impella

<table>
<thead>
<tr>
<th>(n = 26)</th>
<th>Impella</th>
<th>IABP</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI at baseline [L/min/m²]</td>
<td>1.71</td>
<td>1.73</td>
<td></td>
</tr>
<tr>
<td>CI at 4 hours</td>
<td>2.23</td>
<td>2.25</td>
<td>N/A</td>
</tr>
<tr>
<td>LVEF at baseline</td>
<td>27%</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>LVEF at discharge</td>
<td>35%</td>
<td>45%</td>
<td>.34</td>
</tr>
<tr>
<td>PCWP at baseline [mm Hg]</td>
<td>22</td>
<td>22</td>
<td>.34</td>
</tr>
<tr>
<td>PCWP after implantation</td>
<td>19</td>
<td>20</td>
<td>.67</td>
</tr>
<tr>
<td>SVR at baseline [dyns-s-cm-5]</td>
<td>1617</td>
<td>1546</td>
<td></td>
</tr>
<tr>
<td>SVR after implantation</td>
<td>1457</td>
<td>1333</td>
<td>.63</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>46%</td>
<td>46%</td>
<td>.97</td>
</tr>
</tbody>
</table>

Cl = cardiac index, LVEF = left ventricular ejection fraction; PCWP = pulmonary capillary wedge pressure; SVE = systemic vascular resistance.

Comparative studies of IABP and PVADs
IMPRESS trial

- Multicenter, open-label, randomized study
- Primary endpoint: 30-day all-cause mortality
- Secondary endpoint: 6-month mortality
- N=48 patients:
  - Impella CP (n = 24)
  - IABP (n = 24)

Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction

Dagmar M. Ouweneel, MSc,1 Erik Erlisen, MD,2 Krischan D. Sjauw, MD, PhD,3 Ivo M. van Dongen, MD,4 Alexander Hirsch, MD, PhD,5 Erik J.S. Packer, MD,6 Marije Vis, MD, PhD,7 Joanna J. Wykrzykoska, MD, PhD,7 Karel T. Koch, MD, PhD,7 Jan Baan, MD, PhD,7 Robbert J. de Winter, MD, PhD,7 Jan J. Pick, MD, PhD,7 Wim K. Lagrand, MD, PhD,7 Bas A.J.M. de Mol, MD, PhD,7 Jan G.P. Tijssen, PhD,7 José P.S. Henriques, MD, PhD7

Comparative studies of IABP and PVADs
IMPRESS trial

- The majority of patients had experienced cardiac arrest
- All were mechanically ventilated
- Half of all deaths were related to anoxic brain injury
- One-third of deaths in both groups were due to refractory cardiogenic shock

Comparative studies of IABP and PVADs
IMPRESS trial

- No difference in short- or midterm survival
  - 50% or 12/24 patients in each group
- Numerically superior survival in those who received either device before PCI rather than after PCI
  - 25% (6 patients) vs. 53% (19 patients), P = 0.16
- Bleeding occurred more often in Impella-treated patients than in IABP-treated patients
  - 8/24 patients vs. 2/24 patients, respectively

Comparative studies of IABP and PVADs
IMPRESS trial

- Although not adequately powered, it was concluded that the PVAD added no additional benefit over IABP in patients with cardiogenic shock after acute MI
- The same authors conducted a meta-analysis including the only three randomized comparisons (n = 95) of IABP and Impella that yielded similar findings
Comparative studies of IABP and PVADs

Serum lactate levels

- The limitations inherent to small trials and meta-analyses of underpowered studies are obvious
- Each study compared first-line use of IABP with more “powerful” PVADs without endpoints suggesting superior efficacy
- It is important to note that serum lactate levels were similar with or without IABP in the SHOCK II study
- In comparative studies, lactate levels were also similar regardless of device, suggesting that the generalized physiologic effect of IABP and PVADs are comparable


Registry data with PVADs

• In the absence of randomized data, registry data become more important in clarifying the role of PVADs
• Short-term mortality rates for cardiogenic shock have been benchmarked around 40% to 50% for 2 decades
• USpella, Euroshock and cVAD registries including a total of 561 patients describe short-term death rates in excess of 50%
• The registries have not provided a signal for improved outcomes

Current state of IABPs

- IABP remains the most commonly used support device and persists as a reasonable first-line approach
- The introduction of larger-displacement balloon catheters is an important enhancement
- Compared with 40cc catheters, the larger 50cc catheter has demonstrated greater systolic unloading and reduction in filling pressures along with up to twice the relative increase in cardiac output
- In the near term, questions of efficacy are likely to remain unanswered both for the IABP and PVADs
- This reality makes device safety and cost even more critical in determining treatment choices

# Current state of IABPs

Benefits of intra-aortic higher efficacy balloons

<table>
<thead>
<tr>
<th>Features</th>
<th>Patient benefits</th>
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</table>
| Greater hemodynamic support  
50cc vs. 40cc for patient > 5’4” (162cm)  
40cc vs. 34cc for patient 5’-5’4” (152-162 cm) |  
• 25% more blood volume displacement  
• 18% more blood volume displacement |
| Improved unloading and augmentation*  
50cc IAB SENSATION PLUS and MEGA IAB |  
• 15% more diastolic augmentation  
• 58% more systolic unloading |
| 40cc IAB SENSATION PLUS and MEGA IAB |  
• 9% more diastolic augmentation  
• 13% more systolic unloading |
| Proprietary membrane* |  
• Balloon material would better withstand abrasion and fatigue resistance to continually deliver the therapy  
• 43% abrasion resistance  
• Improved fatigue resistance  
• Immediate inflation at start-up |

*Bench testing completed by Getinge. Data on file. Bench test results are not necessarily predictive of clinical results.
Current state of IABPs
Bleeding and vascular complications

- Multiple arterial access points and larger catheter sizes almost exclusively translate into more bleeding and vascular complications
- Contemporary safety data are available for more than 600 patients randomly assigned to IABP in clinical trials
- Supporting its established safety profile, there was no significant increase in either major bleeding or major vascular complications with the IABP

<table>
<thead>
<tr>
<th>Trial</th>
<th>IABP (%)</th>
<th>No IABP (%)</th>
<th>P value</th>
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<tr>
<td>BCIS-1 minor bleeding</td>
<td>15.9</td>
<td>7.3</td>
<td>.02</td>
</tr>
<tr>
<td>BCIS-1 major bleeding</td>
<td>3.3</td>
<td>4.0</td>
<td>.77</td>
</tr>
<tr>
<td>CRISP AMI major bleeding</td>
<td>3.1</td>
<td>1.7</td>
<td>.49</td>
</tr>
<tr>
<td>CRISP AMI major vascular</td>
<td>4.3</td>
<td>1.1</td>
<td>.09</td>
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<tr>
<td>SHOCK II moderate bleeding</td>
<td>17.3</td>
<td>16.4</td>
<td>.77</td>
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<tr>
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Trial enrolment: BCIS-1, n = 301; CRISP AMI, n = 337; SHOCK II, n = 600.

Abbreviation: IABP, Intra-aortic balloon pump.

Costs of care and guidelines

- Additional health care expenses are both reasonable and justifiable for devices with robust clinical benefit
- Novel PVADs may cost 10 to 30 times more than the IABP
- The implications for health care costs are dramatic considering the exponential increase in PVAD use

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<td>+</td>
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<tr>
<td>Cost</td>
<td>$835</td>
<td>$21,131</td>
<td>$23,645</td>
<td>$25,000</td>
</tr>
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Costs of care and guidelines

- The increase in use of novel PVADs, despite lack of demonstrable clinical benefit, has a potentially large effect on health-care expenditure.

- A first-line strategy of IABP with escalation to PVADs could avoid these incremental costs that exceed $2.5 billion at 100% migration.

Costs of care and guidelines

- The neutral results of IABP-SHOCK II weighed heavily on European Society of Cardiology guidelines
- Routine use of the IABP in cardiogenic shock was given a Class III recommendation
- Importantly, the IABP has retained an endorsement (Class IIa) for unstable and cardiogenic shock patients with mechanical complications, and it remains in another recommendation for short-term mechanical support in cardiogenic shock

Costs of care and guidelines

- The IABP is included in recommendations in the latest U.S. guidelines for post-MI shock patients who do not quickly stabilize with pharmacotherapy.

- In the absence of direction from randomized data, the 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on mechanical support, endorsed by the American Heart Association, did not provide specific guidance on device use.


Treatment of cardiogenic shock

Device algorithm

Summary

• The IABP is unique in its safety profile, cost efficiency and breadth of experience, and retains its position as the most widely used hemodynamic support device
• Although a direct relationship between device power and improved outcomes is intuitive, it is, as of yet, unproven
• Higher-flow PVADs may ultimately be best to solve the challenges of hemodynamic collapse
• It is most likely that the IABP and PVADs will each play complementary roles in shock and acute care
• Further research is needed to change the paradigm CS
• Could earlier initiation of MCS be the answer?
Questions?

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