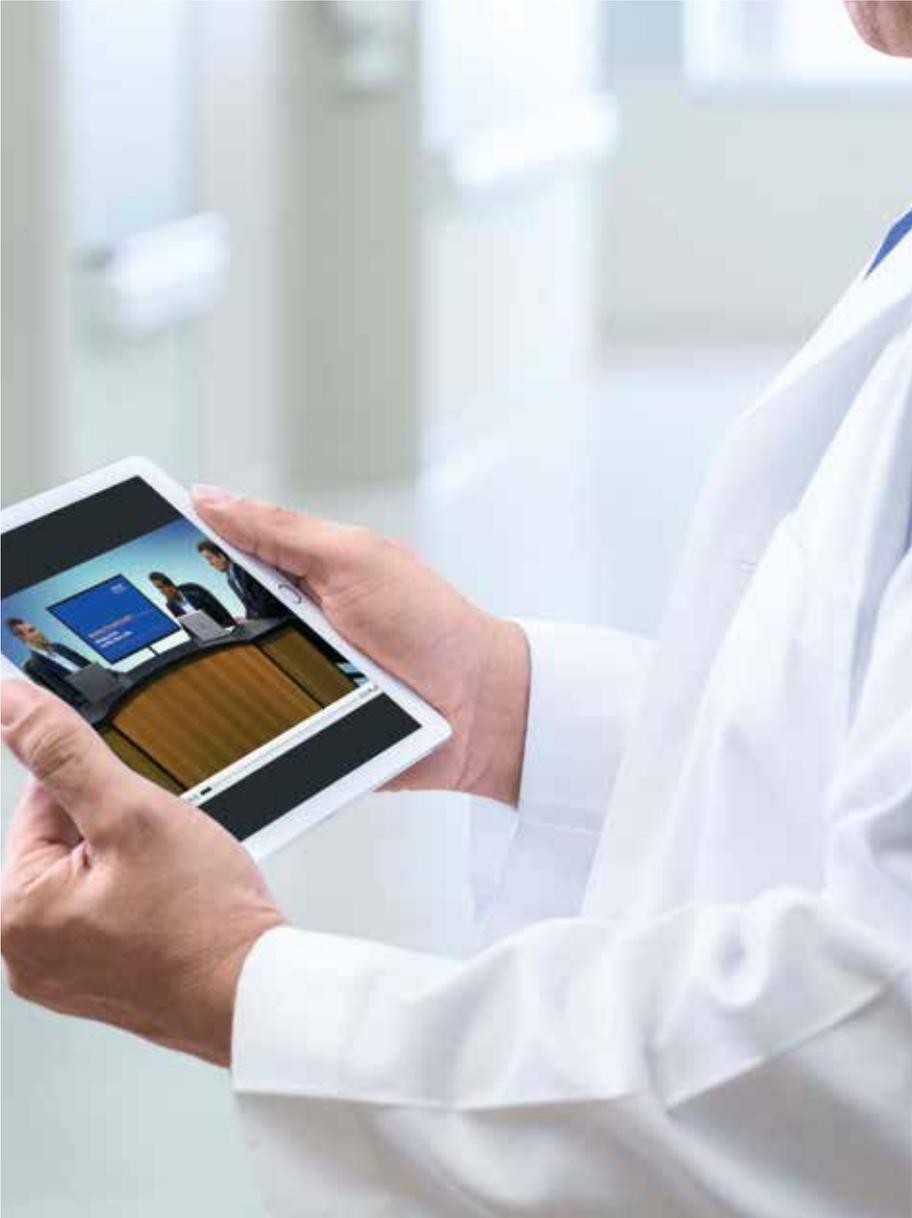

Mechanical Circulatory Support
Bringing Clarity: The Why, When, & Who

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Introduction

The intra-aortic balloon pump (IABP) has long been the first-line choice for mechanical circulatory support around the world due to its clinical efficacy, safety profile across a broad range of patient care scenarios, and low cost. Recently, debate regarding the IABP has centered on the discrepant results obtained from randomized, controlled trials (RCTs) versus the benefits observed by clinicians in the decades of clinical practice. This series of educational programs provides a review of the physiological principles behind currently available circulatory support therapies, ranging from inotropes and IABP therapy to percutaneous left ventricular assist devices (pVADs) and extracorporeal pumps. The programs will also discuss the dichotomy between trial results and clinical practice, and provide case examples that focus on tailoring mechanical circulatory support strategies for the individual patient.

- **Module 1: The Critical Science: Understanding the ABCs of Mechanical Circulatory Support**
This module presents a systematic approach to evaluating the physiological principles behind available mechanical circulatory support devices and how to select which device based on the physiological needs of the individual patient
- **Module 2: The Clinical Enigma: Randomized Trials vs. Clinical Practice**
This module discusses why randomized trials of IABP have failed to reach their primary endpoints despite decades of data showing benefits of such treatment and the emerging science that demonstrates which patients may most benefit from IABP
- **Module 3: Real World Application: The Why, When, & Who**
This module illustrates the range of available support methods and the importance of tailoring the support method to the evolving patient clinical scenario rather than to a broad diagnostic category

This booklet complements the educational video series found at www.maquet.com

I invite you to view the programs.

Simon Redwood, MD, FRCP, FACC, FSCAI

Professor of Interventional Cardiology

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Champions of the Cath Lab

Simon Redwood, MD, FRCP, FACC, FSCAI

Professor Redwood is Senior Lecturer/ Consultant Interventional Cardiologist and Director of the Cardiac Catheter labs at Guy's and St Thomas' Hospital in London, one of the highest-volume catheter labs in the UK. He is also Lead Clinician for Research and Development and is President of the British Cardiovascular Intervention Society (BCIS). He is a member of the Interventional Procedures Advisory Committee for the National Institute of Clinical Evidence (NICE) and International Editorial Board member for the journal Heart. He is trained in all aspects of adult interventional cardiology.



Divaka Perera, MA, MD, FRCP

Dr. Perera is a Reader in Interventional Cardiology and Senior Lecturer in Cardiology for King's College Hospital and an Interventional Cardiologist at Guy's and St Thomas' Hospital in London. In 2008, he received a five-year clinical senior lectureship award from the Department of Health, Higher Education Funding Council for England (HEFCE) and the UK Clinical Research Collaboration (UKCRC). At the same time, he was also appointed to the post of Consultant Cardiologist at Guy's and St Thomas'.



In addition to his clinical and research roles, Dr. Perera teaches undergraduate medical students and supervises postgraduate researchers toward MSc, MD, and PhD degrees at King's College London.

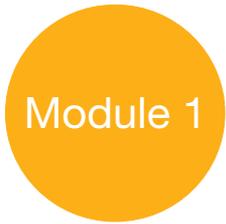
Nico H.J. Pijls, MD, PhD

Professor Nico Pijls is a Professor of Biomedical Engineering and Cardiology at the Catherina Hospital and the University of Technology in Eindhoven. In his role in biomedical engineering, his research has covered measurements in cardiac and coronary hemodynamics. He was the co-investigator for the FAME trials on FFR-guided PCI in detecting ischemia which led to an upgrade of the ESC guidelines in 2014 to a Class I level of evidence A. He is an Interventional Cardiologist responsible for the day-to-day care of cardiac patients at the Eindhoven Heart Center, Catherina Hospital.



In addition to his clinical and research roles, Professor Pijls also teaches physicians in cardiology. He is the author of three published books on diseases of the coronary artery.

Disclosure: All presenters have a speaker agreement with Maquet.



Module 1

The Critical Science

The Critical Science: **Understanding the ABCs of Mechanical Circulatory Support**

Divaka Perera, MA, MD, FRCP
Guy's and St Thomas' Hospital, London

The available methods for supporting the circulation differ in terms of three main factors:

- A.** Myocardial protection provided
- B.** Organ (tissue) perfusion achieved
- C.** Safety and ease of use

The relative strengths and weaknesses of each strategy must be considered when making decisions for individual patients.

Goals of Mechanical Circulatory Support

A. Myocardial Protection

This aspect represents the likelihood of overcoming ischemia, that is, tilting the balance favorably between oxygen demand (driven by heart rate, contractility, and afterload) and oxygen supply (driven by the diastolic pressure–time integral, microvascular resistance, and coronary artery patency).

B. Organ Perfusion

This aspect reflects maximizing blood flow to tissues. Although mean arterial pressure (MAP) is the main determinant of tissue blood flow, local tissue vascular resistance (TVR) also plays a role. Many strategies that increase MAP work by increasing peripheral vascular resistance and can have the counteractive effect of increasing TVR. Improving cardiac output (CO) is also the primary means of improving tissue perfusion. CO is the product of heart rate and stroke volume, the latter representing the difference between end-diastolic volume (determined by filling pressure and cardiac compliance) and end-systolic volume (determined by afterload and contractility).

C. Safety/Ease of Use

This dual aspect reflects the risks of major complications (bleeding, access site/vascular, and cerebrovascular) as well as the feasibility of use (local availability, deployment speed, and the expertise required for initiation and monitoring).

Circulatory Support Strategies

1. Inotropic Drugs

All of the first-line inotropic drugs commonly used for circulatory support achieve the goal of increasing CO. This benefit can be offset, however, by the costs of increased myocardial oxygen demand and varied effects on TVR.

At a minimum, given the drugs' universal availability and the ability to initiate therapy rapidly, inotropic drugs can be used to stabilize patients until a more definitive therapy can be initiated. Continued use of such drugs for a prolonged period of time is generally not considered a preferred strategy.

Effects of Inotropic Drugs on Hemodynamics

Drug	Mechanism	Effects			
		CO	SVR	MAP	TVR
Dobutamine	DA β 1 β 2 agonist	↑↑	↓	↑↓	↓↑
Epinephrine	α 1 β 1/2 agonist	↑↑	↑↑	↑↑	↑
Norepinephrine	α 1 β 1/2 agonist	~	↑↑	↑↑	↑↑
Levosimendan	Ca ⁺⁺ sensitizer	↑↑	↓↓	~	↓
Milrinone	PDE inhibitor	↑↑	↓↓	~	↓

Ca⁺⁺: calcium ion; CO: cardiac output; DA: dopamine; MAP: mean arterial pressure; PDE: phosphodiesterase 3; SVR: systemic vascular resistance; TVR: tissue vascular resistance.

2. Intra-aortic Balloon Pump (IABP)

The IABP has been the most commonly used circulatory support device for almost 50 years. It consists of a balloon catheter, which is typically inserted percutaneously into the femoral artery and advanced into the descending thoracic aorta, and a pump that controls balloon inflation/deflation. The balloon is inflated as diastole begins, augmenting aortic pressure and thus coronary perfusion during the diastolic period. A forgotten mode of action is when the balloon is deflated as diastole ends, reducing end-diastolic and early systolic pressure in the aorta. This reduction in the two pressures decreases afterload and increases cardiac output (Figure 1). Thus, the sum total of effects during inflation and deflation act to increase blood (oxygen) supply as well as reduce demand.

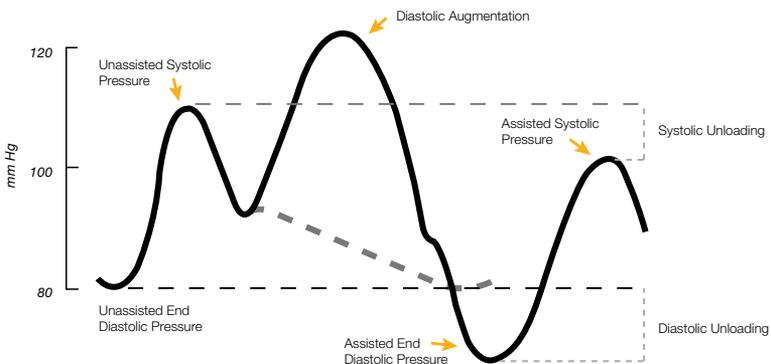


Figure 1: Arterial pressure waveform effects with IABP inflation and deflation

The potential benefits of the IABP may be modulated by the process of autoregulation, i.e., the heart's ability to maintain constant coronary blood flow despite changes in perfusion pressure. In a small study of patients with intact autoregulation undergoing high-risk percutaneous coronary intervention (PCI), the increased diastolic pressure achieved with the IABP was offset by increases in microvascular resistance, with little to no change in coronary flow.¹ However, when autoregulation was disabled, the IABP using the 50cc IAB was associated with greatly improved flow and perfusion. Thus, this support method might be of greatest benefit when the microcirculatory reserve is exhausted or disrupted, as is the case with cardiogenic shock, persistent hypotension, or persistent coronary ischemia due to vessel occlusion or spasm (Figure 2).¹

Disabled Autoregulation

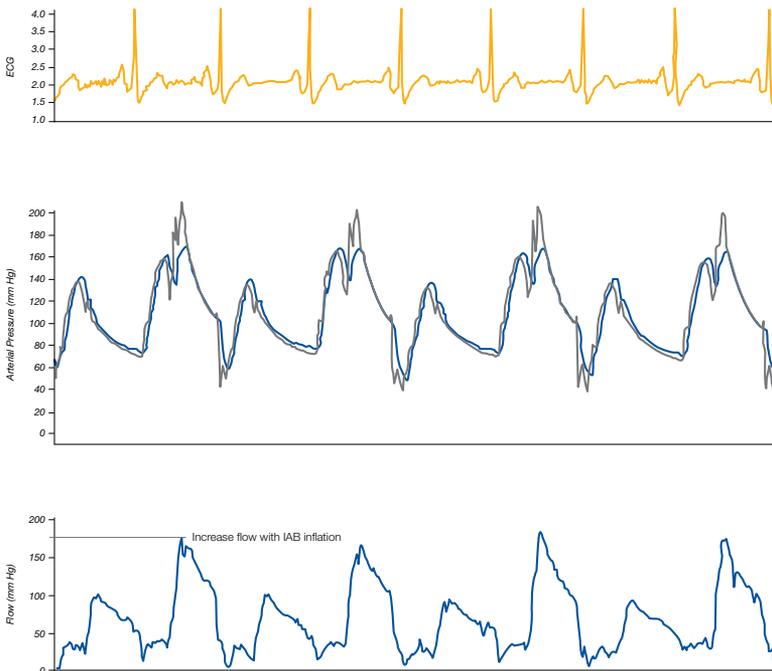
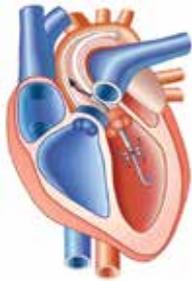


Figure 2: IABP effects with disabled autoregulation

The IABP is widely available and familiar to most practitioners in catheterization facilities. Safety concerns have typically involved bleeding risk and vascular complications. We recently analyzed all randomized trials of the IABP versus control that enrolled >100 patients (seven studies; 2095 total patients).² Rates of vascular complications and of device-related bleeding did not differ significantly with IABP use, even in situations that would have required rapid insertion of the device (e.g., acute myocardial infarction or cardiogenic shock). Although some clinicians may have concerns about excess risk with the IABP, the data from randomized trials do not support this. Continued decreases in IABP catheter sizes and refinements in insertion techniques no doubt have contributed to the diminishing potential for adverse events.

3. Percutaneous Left Ventricular Assist Devices (pVADs)

The Impella® 2.5 device (Abiomed, Aachen, Germany) is an intracorporeal, catheter-based, impeller-driven, axial flow pump. It is typically inserted into the femoral artery and then advanced into the left ventricle. There the device pumps blood continuously and directly into the ascending aorta, thus providing direct, nonpulsatile ventricular unloading. The device can produce aortic flow of 2.5-3.5 L/min with the 12-14 Fr pump motor, and it is FDA-approved for use for up to 6 hours.³



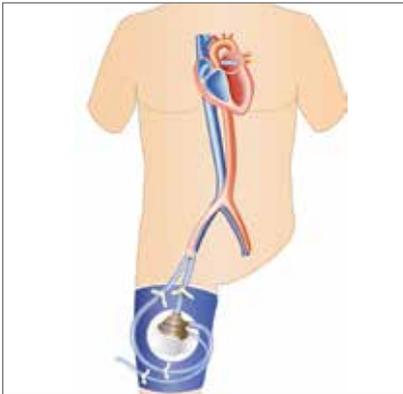
A meta-analysis has examined hemodynamic measures and clinical outcomes with the use of percutaneous pVADs versus IABPs in cardiogenic shock.⁴ One trial used the Impella 2.5 device, and two trials evaluated the TandemHeart device. Use of pVADs was associated with superior hemodynamic support compared with the IABP among the 100 patients analyzed. However, these findings did not translate into improved 30-day survival (Figure 3), with no difference in leg ischemia (Figure 4), and the use of a TandemHeart LVAD was associated with more than twice the risk of bleeding compared with the IABP (bleeding was not reported for the Impella study).⁴ (See Figure 5.)

Myocardial protection is achieved with this method by decreasing afterload and thus reducing oxygen demand. Specific effects on myocardial perfusion are unknown at present. This device also improves cardiac output without increasing TVR, thus enhancing tissue perfusion.

The Impella devices are relatively safe and easy to use, but the risks of bleeding and vascular complications increase with larger-bore access. There is also a substantial learning curve for insertion and post-catheterization laboratory management of these devices.

4. Extracorporeal Pumps

The TandemHeart System (CardiacAssist, Inc., Pittsburgh, PA, USA) is a left atrium-to-femoral artery temporary circulatory support device driven by a low-speed, centrifugal continuous-flow pump.⁵ The pump draws oxygenated blood from the left atrium and returns the blood to one or both femoral arteries via the transeptal cannula completely bypassing the left ventricle. The pump can deliver up to 5.0 L/min of flow percutaneously.⁵

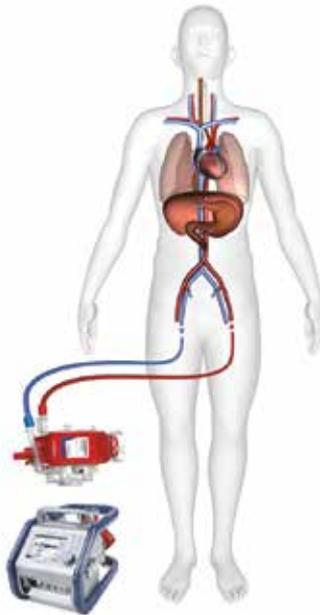


The TandemHeart device improves cardiac output and thus tissue perfusion. As noted, the risk of bleeding also was significantly higher with this device versus the IABP in two small studies.^{6,7} This likely reflects the need for large-bore arterial/venous access. The device also requires transeptal puncture, which carries the risk of thromboembolic and mechanical complications. Insertion of the TandemHeart device is not as familiar for many cardiologists who have not performed transeptal puncture.

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) or extracorporeal life support (ECLS) draws deoxygenated blood from a central vein or the right atrium, passes the blood through an external membrane system for gas exchange, and then returns the oxygenated blood into a major artery (typically the aorta via a femoral artery).

ECMO/ECLS improves cardiac output and tissue perfusion however, afterload/myocardial oxygen demand is increased. The effect on coronary perfusion is uncertain.

The safety and complexity of ECMO/ECLS are also similar to those of the TandemHeart device. Both modalities require large-bore vascular access, and they are more invasive procedures. Vascular and bleeding risks are similarly increased compared with the IABP. As yet, there have not been properly powered randomized comparisons of these strategies.



Summary

Each method of circulatory support should be assessed by its effects on myocardial oxygen supply and demand, tissue perfusion, and safety/ease of use. The table below summarizes the relative strengths and weaknesses of each approach.

	Myocardial Protection		Tissue Perfusion	Ease of Use
	Supply	Demand		
Inotropic drugs	+/-	-	+/-	++++
IABP	+	+	+	+++
Impella	?	++	++	++
TandemHeart	?	-	++++	+
VA-ECMO	?	-	+++++	-

+: beneficial effect; -: negative effect; ?: missing/equivocal data

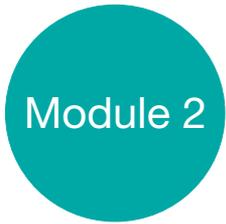
Selecting a Support Strategy

When faced with a given patient, the clinician has two options when selecting a circulatory support method:

1. Using the broad diagnosis (e.g., myocardial infarction, cardiogenic shock, high-risk PCI)
2. Using the patient's individual physiology and care environment

An argument against the first approach comes from the randomized trials that have compared the IABP versus control or Impella device for patients categorized by a broad diagnostic label, high-risk PCI^{8,9} and IABP versus control for acute myocardial infarction with¹⁰ and without¹¹ cardiogenic shock. None of these trials showed a significant difference in the primary endpoint by treatment assignment, suggesting that the broad diagnosis might not be a reliable basis for making support decisions.

Tailored therapy is, in principle, a better option. If a particular patient has a greater need for myocardial protection, for example, then he or she might be better served by the IABP rather than inotropic drug therapy. If tissue perfusion is of greater concern, then a pVAD or VA-ECMO/ECLS might be the better option. If ease of use is the primary concern, such as when an unstable patient needs immediate treatment, then inotropic drugs and the more familiar support devices, like the IABP, will play the major role.



Module 2

The Clinical Enigma

The Clinical Enigma: **Randomized Trials vs. Clinical Practice**

Nico H.J. Pijls, MD, PhD
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The use of an intra-aortic balloon pump (IABP) has produced dramatic clinical improvement in select patients, but this improvement has not been observed universally. Similarly, many retrospective studies have reported benefits of IABP use, but recent prospective, randomized controlled studies have failed to reach their primary endpoints. This module reviews the data regarding these differences and examines the emerging science of selecting which patients might derive benefit from the IABP.

Evidence from Randomized, Controlled Trials

IABP-SHOCK II¹⁰

In this open-label, multicenter trial, 600 patients with acute myocardial infarction (MI) complicated by cardiogenic shock for whom percutaneous coronary intervention (PCI) was planned were randomized to receive IABP therapy or no IABP. The incidence of the primary efficacy endpoint, 30-day all-cause mortality, did not differ by treatment assignment: 39.7% with the IABP vs. 41.3% without IABP ($P=0.69$). The treatment groups likewise did not differ in the incidence of secondary endpoints, in-hospital bleeding, ischemic or vascular complications (Table 1), or process-of-care measures.

	IABP (n=300)	Control (n=298)	P
Stroke	2 (0.7%)	5 (1.7%)	0.28
Gusto bleeding:			
Life-threatening/severe	10 (3.3%)	13 (4.4%)	0.51
Moderate	52 (17.3%)	49 (16.4%)	0.77
Peripheral ischemic complication*	13 (4.3%)	10 (3.4%)	0.53
Sepsis	47 (15.7%)	61 (20.5%)	0.15

*Requiring intervention.

Table 1: In-Hospital Safety in the IABP-SHOCK II Study

The high rate of crossover in this trial might have produced a positive bias in favor of the control (PCI-only) group and a negative bias for the IABP treatment group. In all, 10% of the control patients underwent IABP insertion, and 7.4% received a left ventricular assist device (LVAD). (This is similar to the 12% crossover rate seen in the randomized BCIS-1 trial of patients with MI but not cardiogenic shock.⁸) In contrast, 4.3% of the IABP group failed to receive the assigned treatment, most often because they died before the planned insertion of the IABP, and 3.7% received an LVAD.¹⁰ Thus, the sickest patients in the control group received additional treatment, reflecting a belief on the part of the investigators that IABP would be of value in this situation (so-called *selective crossover bias*¹²). At the same time, the sickest patients in the IABP group, who might have derived the greatest benefit from such treatment, died before they could have the device inserted. This, in effect, translates into a negative bias for the treatment group. If the use of an additional support device had been included in a composite primary endpoint, the trial would have shown a positive effect for the IABP.

The timing of IABP insertion relative to PCI performance also could have been a factor. In a previous study of patients with MI and cardiogenic shock undergoing primary PCI, those who had had the IABP inserted before the procedure had significantly lower in-hospital mortality and major adverse cardiac and cerebrovascular events.¹³ In the SHOCK II study, 87% of the patients in the IABP group had the device inserted after PCI, but mortality did not differ between these patients and those who had the device inserted before PCI (36.8% vs. 36.4%, respectively; $P=0.96$).

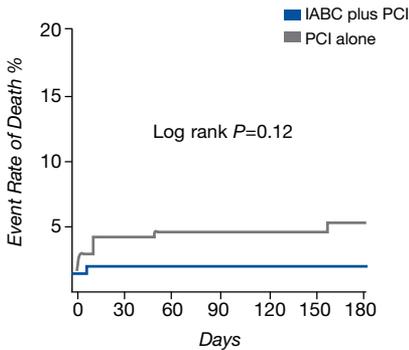
CRISP-AMI¹¹

This multicenter, open-label, controlled trial randomized 337 patients with acute anterior MI of <6 hours' duration and without cardiogenic shock to receive primary PCI alone or primary PCI with an IABP (started before the procedure and continued for at least 12 hours). The primary endpoint was infarct size, defined as the percentage of left ventricular mass measured with magnetic resonance imaging (MRI) 3–5 days after PCI. Secondary endpoints included all-cause mortality at 6 months and major vascular complications and major bleeding at 30 days.

The treatment groups did not differ significantly in terms of infarct size, major vascular complications, or major bleeding. By 6 months, three patients in the IABP group and nine patients in the PCI-only group had died (1.9% vs. 5.2%, respectively; $P=0.12$; see Figure 1). For the exploratory endpoint of death, shock, or new/worsening heart failure, there was a significant benefit with IABP treatment versus PCI alone (eight events [5%] vs. 21 events [12%], respectively; $P=0.03$).

The trial had three main limitations that served to dilute the possible benefits of the IABP. First, the inclusion criteria were not particularly robust. The majority of patients (56%) had a limited amount of myocardium at risk, making a benefit harder to detect. Second, if adequate reflow is present after PCI, as was the case in many patients, then a good outcome is more likely in any event. The collective effects of these factors resulted in a severely underpowered study. Last, as in the SHOCK II and BCIS-1 studies, selective crossover also occurred frequently in the CRISP-AMI; in all, 8.5% of the PCI-only group received IABP therapy, confounding the analysis.

Event Rate of Death from 0 to 180 Days



No. at risk

PCI alone	174	167	165	165	165	165	164
IABP plus PCI	157	154	153	153	153	153	153

Figure 1: IABC indicates intra-aortic balloon counterpulsation; PCI, percutaneous coronary intervention.

Of note, in a subgroup analysis from this study, 6-month mortality was found to be significantly lower with the use of the IABP in patients with a large MI (n=149; 44% of the overall study population) or persistent ischemia (n=36; 11% of the study population)—no such patients in the PCI-IABP group died versus 24% in the PCI-only group $P=0.046$ (Figure 2).¹⁴

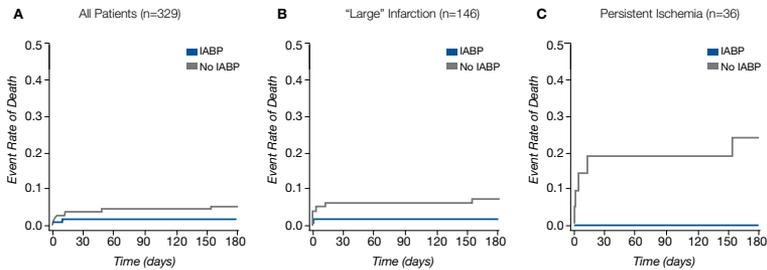


Figure 2: CRISP-AMI subgroup analysis

Lessons from Randomized Studies

Study Design and Analysis

Intention-to-treat (ITT) analyses may not be appropriate for studies of devices such as the IABP, for several reasons. Among the prerequisites for ITT analyses are that the study should be double-blind, include large numbers of patients, have relatively rare events compared with the sample sizes, and allow few and nonselective crossovers (to minimize confounding). All of these criteria are difficult or impossible to incorporate into studies of IABP use. In the particular case of crossovers, if they are driven by failure of the “treatment” strategy, positive bias in favor of the control group and negative bias for the “device” group are unavoidable, unless crossover is considered part of the primary endpoint.

The logical alternative to ITT analysis is the “as-treated” approach, which the SHOCK II study examined in addition to the ITT analysis.¹⁵ Results did not differ substantially between the analysis methods in this study. In general, however, when crossover rates are high and asymmetrical (as in IABP-SHOCK II), the benefit of randomization (balance in baseline characteristics) is lost. That is, the “worst” patients from the control group are transferred into the “treatment” group. In such scenarios, an absence of difference in outcomes between groups might actually indicate superiority of the treatment.

In the randomized, controlled trials of the IABP versus no IABP, serious negative bias and confounding were present, thus by definition masking potentially positive effects of the device. These are fundamental problems in open-label studies of unstable patients with high mortality risk. The only way to circumvent these issues is to forbid crossover, which is difficult to do from an ethical view, or add it as a component of a primary endpoint.

Optimal Use of the IABP

Under normal physiological circumstances, autoregulation can ameliorate the effects of the IABP (increased diastolic perfusion pressure resulting in increased coronary blood flow/oxygen supply). Thus, the IABP would not be expected to have a noticeable effect on coronary blood flow in such cases. When autoregulation has been exhausted, however, coronary blood flow would be expected to increase in direct proportion to IABP-related increases in diastolic perfusion pressure (Figure 3).

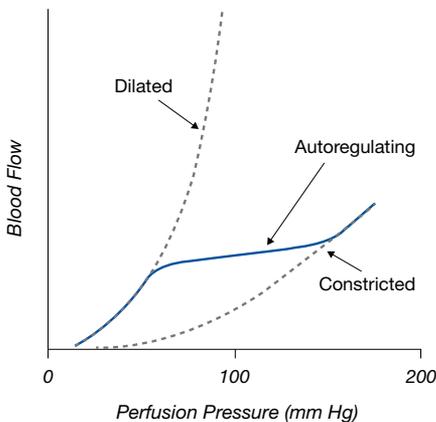


Figure 3: Coronary autoregulation

Courtesy of Richard E. Klabunde, PhD

<http://www.cvphysiology.com/Blood%20Flow/BF004.htm>

Situations of Impaired Autoregulation

- Ongoing myocardial ischemia:
 - Acute phase of MI with insufficient or no reflow
 - Post cardiac surgery with myocardial stunning
- Low diastolic blood pressure (<60 mm Hg)
- Significant stenosis

In observational studies, the IABP has been associated with better outcomes in patients who have viable myocardium and who have persistent ischemia despite the presence of an unobstructed coronary artery.¹⁶ This phenomenon has been validated in an *ex vivo*, beating-heart model in pigs that allows independent control of afterload (blood pressure), preload (left arterial pressure), contractility, arterial oxygen saturation, and heart rate.¹⁷ The model thus permits manipulation of autoregulation and induction of pump failure, cardiogenic shock, and large MI with persistent ischemia.

In all scenarios tested, IABP use increased coronary blood flow and cardiac output. The induced effects were significantly greater during times of myocardial ischemia. In addition, myocardial oxygen consumption increased when blood flow was increased to the ischemic area, whereas consumption remained stable (despite increased blood flow) when the tissue was already perfused. In effect, the IABP reversed and stabilized the progressive hemodynamic deterioration caused by oxygen insufficiency (Figure 4).

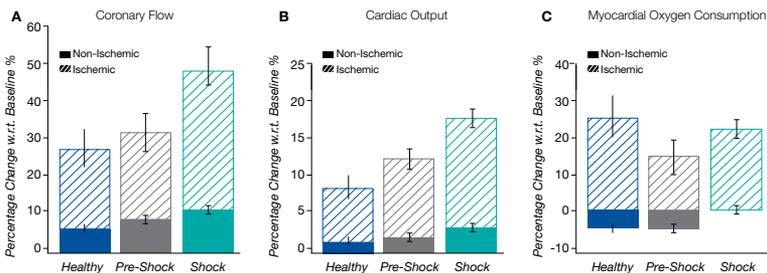


Figure 4: Effects of IABP on coronary blood flow/cardiac output/myocardial oxygen consumption in pig hearts with and without persistent ischemia¹⁷

Summary

Large randomized, controlled trials that have shown negative results for IABP-SHOCK II and CRISP-AMI are limited by inappropriately broad inclusion criteria and by inappropriate statistical analyses. As a result, these trials should be considered inconclusive. In fact, alternative methods of analyzing these trial data have produced indicators of efficacy with IABP use in certain scenarios.

The IABP may be particularly useful in patients with viable myocardium who have persistent ischemia despite the presence of a patent coronary artery.¹⁶ This situation includes the cases of no reflow after successful PCI for acute MI (occurring in 2.3% of the patients in a very large, contemporary registry)¹⁸ and stunning after coronary artery bypass grafting. In such patients, IABP use might improve blood flow to and oxygen use by cardiac myocytes, thus increasing contractility and cardiac output, salvaging myocardium, and perhaps improving long-term outcomes.

This hypothesis is being tested in the Survival in Extensive Myocardial Infarction with PERSistent ischemia Following IABP study (SEMPER FI; [clinicaltrials.gov #NCT02125526](https://clinicaltrials.gov/ct2/show/study/NCT02125526)).¹⁹ The trial is randomizing 100 patients undergoing primary PCI for large acute MI to receive the IABP or no IABP, but only if they show <50% ST-segment resolution soon after PCI. The primary endpoint is the 6-month composite of all-cause mortality, use of mechanical support for hemodynamic deterioration, or hospital admission for heart failure. All-cause mortality at 30 days is also being assessed.

Of note, PCI-only patients are not being permitted to cross over to IABP. Data from this trial should clarify the possible benefits of IABP use in patients with persistent ischemia in the presence of patent coronary arteries.



Module 3

Real World Application

Real World Application: **The Why, When, & Who**

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Through a series of case studies, this module illustrates the range of available support methods and the importance of tailoring hemodynamic support strategies to the evolving patient clinical scenario rather than to a broad diagnostic category.

Case #1

A 74-year-old woman had exertional angina and dyspnea for 1 week, which suddenly became much worse 4–5 hours before transport to the hospital. Upon arrival, she had cold, clammy skin; pulmonary congestion; hypotension (90/50 mm Hg); tachycardia; respiratory distress; and reduced oxygen saturation. Electrocardiography revealed Q-waves over the anterior wall and persistent ST-segment elevation (Figure 1).

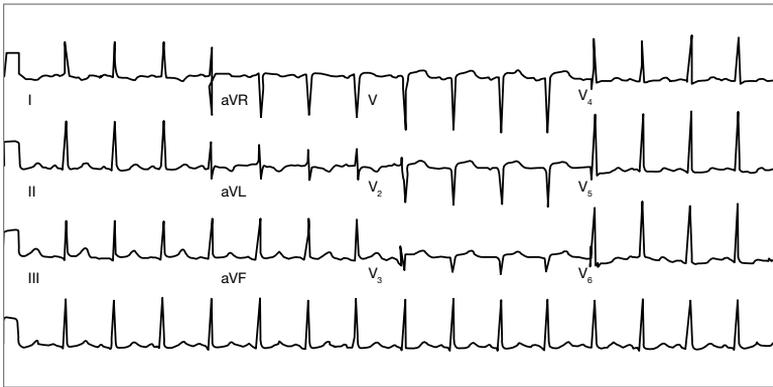


Figure 1: Admission ECG

The initial diagnosis was subacute anterior wall myocardial infarction (MI) with cardiogenic shock.

Angiography showed severe multivessel coronary artery disease. Subtotal stenosis was present in the right coronary artery (RCA; see Figure 2), which was dominant, with subtotal stenotic lesions in the left anterior descending coronary artery (LAD; see Figure 3), the likely culprit lesions for the MI. An echocardiogram performed in the catheterization laboratory showed left ventricular dysfunction (LVD) and severe mitral valve regurgitation (Figure 4).

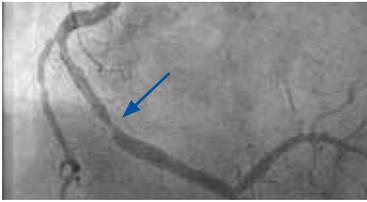


Figure 2: RCA occlusion

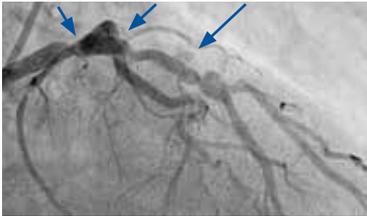


Figure 3: LAD occlusions

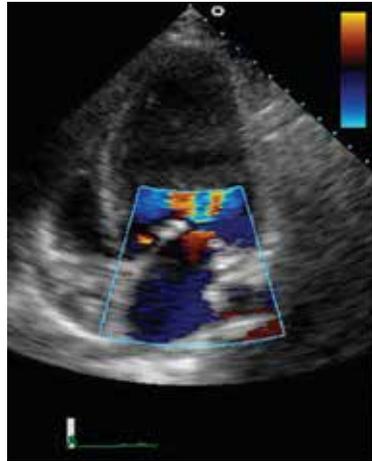


Figure 4: ECHO mitral valve regurgitation

The IABP was inserted prior to this high-risk percutaneous coronary intervention (PCI) procedure. The patient then underwent successful PCI and stents were deployed in the RCA and the LAD (Figures 5a and 5b).



Figure 5a: RCA post-PCI



Figure 5b: LAD post-PCI

She received glycoprotein IIb/IIIa inhibition perioperatively, along with inotropic support for 1 day. The IABP was left in place for 24 hours, after which the patient was successfully weaned from the device.

At 2-year follow-up, the patient had no cardiac complaints, and her ejection fraction was 53%. Mitral regurgitation was still present but had improved, being of mild to moderate severity.

Discussion

Because of the patient's subtotal lesion in the RCA, autoregulation in that territory was exhausted during the MI. The territory of the RCA was required to become hyperkinetic to compensate, resulting in secondary ischemia. In effect, in the territory of the LCA and the contralateral portion of the myocardium, autoregulation was exhausted.

The IABP was inserted prior to the high-risk PCI procedure due to the extensive amount of myocardium at risk, ongoing ischemia in the right and left territory, as well as the indication for acute MI. IABP augments coronary flow, as well as provides LV unloading, which was useful for the patient's mitral regurgitation.

An IABP rather than an Impella or other percutaneous left ventricular assist device (pVAD) was selected for the following reasons:

1. Of paramount importance was the ischemia in the patient's right and left coronary territories, which was likely to include some microvascular dysfunction. Given that blood flow in the coronary arteries is directly related to diastolic perfusion pressure in patients with impaired autoregulation, the increase in diastolic pressure characteristic of the IABP was thought to offer the patient the greatest benefit for myocardial protection.
2. Another pVAD such as the Impella device could have improved cardiac output; however, the coronary hypoperfusion would not have been treated as effectively.

Improving myocardial ischemia indirectly improves the cardiac output but, more importantly, may salvage the myocardium. Improved myocardial salvage may explain, at least in part, the long-term survival benefits observed with elective IABP use in the BCIS-1 study.²⁰

Case #2

A 55-year-old woman presented late (>24 hours) after onset of anginal symptoms. She had a history of hypertension but no other cardiovascular conditions. Upon arrival, her systolic blood pressure was 90 mm Hg, and she showed early signs of pulmonary edema. The ECG showed extensive anterolateral ST-segment elevation.

Echocardiography revealed left ventricular dysfunction and the presence of a large ventricular septal defect (VSD) (Figure 1a). Subsequent angiography showed occlusion of the proximal LAD (Figure 1b). The decision was made to support the patient hemodynamically with an IABP while preparing for surgical intervention for the LAD lesion and the VSD. The assumption was that the patient's symptoms were the result of ongoing ischemia and mechanical issues arising from the MI, although it was equally likely that the infarction had already been completed and that the VSD was the cause of her current symptoms.

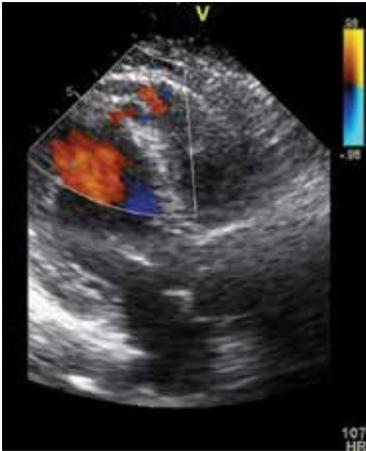


Figure 1a: ECHO showing VSD



Figure 1b: LAD occlusion

The IABP was inserted prior to intervention, after which the patient underwent thrombus aspiration of the LAD to restore blood flow in the artery. No PCI balloon dilatation or stent deployment was performed, since bypass surgery was planned (Figure 2).



Figure 2: LAD post thrombectomy

The following morning, she had been taken off all inotropic support and was very stable with IABP treatment. The surgical team then requested that surgery be delayed for a few days, if possible, so that the patient could receive support longer. On Day 6, the intensive care team thought that the patient was well enough to have

the IABP removed; however, as the weaning process started, she developed significant pulmonary edema. Chest radiography at that time showed extensive alveolar shadowing.

The IABP was restarted immediately, along with a short course of inotropic drugs, and the patient restabilized. Within 24 hours of the weaning attempt, she underwent successful surgical repair of the VSD.

Discussion

Although the patient appeared to have three potential indications for IABP support at first (VSD, cardiogenic shock, and ischemia after MI), the attempt to wean the patient from the IABP demonstrated that the VSD was the factor most responsive to use of the device.

Given the initial presentation, the need for afterload reduction as long as the VSD exists is of extreme importance. A primary reason for selecting the IABP over a device such as the Impella was to provide continuous hemodynamic support until surgery could be performed, (the current FDA-approved duration of support using the Impella device is only 6 hours). The IABP was able to offer this support with a lower risk of complications.

Case #3

A 49-year-old man presented initially, after having chest pain for several hours, at a facility that lacked a catheterization laboratory. His medical history was positive for impaired glucose tolerance and family history of ischemic heart disease (IHD), but he was otherwise healthy. Several hours later, he was transferred to a facility that had PCI capability.

When he arrived at the tertiary facility, he was found to have pulmonary edema and was showing early signs of shock. ECG revealed significant anterior ST-segment elevation in leads V 1-5. His oxygen saturation was only 80%, and although his blood pressure remained at 120/70 mm Hg, he was tachycardic. The diagnosis was made of acute myocardial infarction (AMI) with incipient cardiogenic shock. The patient underwent immediate angiography, which showed occlusion of the proximal LAD and relative unobstruction of the circumflex artery and RCA (Figure 1). Because of the patient's poor hemodynamic situation, the decision was made to insert an IABP before any intervention was undertaken.

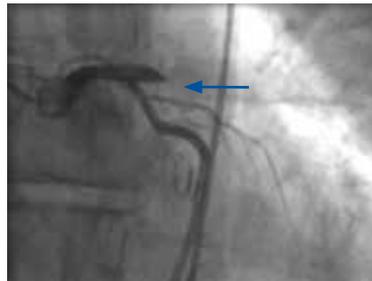


Figure 1: Diagnostic angiogram

The patient underwent extraction of a significant thrombus burden and deployment of a drug-eluting stent in the LAD (Figure 2). He also received adjunctive glycoprotein IIb/IIIa inhibitor therapy.

After PCI, blood flow in the LAD was only TIMI Grade 2, perhaps indicating previous distal embolization and thus an etiology for the cardiogenic shock. In addition, the patient's ST-segment elevation was only minimally resolved.



Figure 2: Post-PCI angiogram

Upon transfer to the coronary care unit, the patient was found to have severe left ventricular dysfunction, despite his having only the single lesion in the LAD. He was initially managed with IABP support, but his clinical situation began to deteriorate over the next 24 hours. Urine output decreased, and lactate levels increased. A dobutamine infusion was then started, but his condition did not improve.

The decision was made to escalate therapy, to provide more support for tissue perfusion. The patient returned to the catheterization laboratory and underwent insertion of an Impella 2.5 device. Again, he appeared stabilized for a short time, after which his urine output decreased dramatically. Treatment was further escalated, with the patient undergoing implantation of a biventricular assist device and subsequent transfer to a facility to await heart transplantation. After successful transplantation, he remains alive and well.

Discussion

In this case, treatment was delayed by several hours because the patient was not transported immediately to a facility that could perform angiography and PCI. Despite the formation of networks offering PCI services, delayed treatment is still the case in many areas around the world. This can carry major implications for myocardial salvage and clinical outcomes.

The reason for this patient's severe LVD remained unclear, given the presence of single-vessel coronary disease. A second pathology might have been present, but regardless of the etiology of the dysfunction, the end result in this patient was the need for escalating support.

After 24 hours of postprocedural IABP therapy, dobutamine was given in an attempt to completely resolve the patient's hemodynamic situation. Such a strategy has the advantage of being readily available and simple to administer. However, inotropic agents have a lesser effect on tissue perfusion than does the IABP, and the patient's lactate level was already elevated, most likely reducing the drug's potential efficacy.

Levosimendan might have represented a viable alternative to dobutamine for this patient, given that levosimendan increases cardiac contractility without also increasing tissue resistance.

When a brief trial of inotropic therapy proved to be inadequate, mechanical support was escalated from an IABP to an Impella device, followed by biventricular assist device implantation. Alternative approaches could have included earlier use of the more invasive extracorporeal membrane oxygenation (ECMO).

Conclusions

These cases illustrate the range of complementary therapies that are available for hemodynamic support, as well as the need for continued tailoring of the treatment approach in response to an evolving clinical situation.

Large randomized, controlled trials that showed negative results for the IABP were limited by overly broad inclusion criteria, masking the specific situations in which the device may be of particular value. It is therefore critical to consider the individual patient's history and physiology when determining the primary goal of support. In cases where myocardial protection, tissue perfusion, and ease of use are of greatest importance, the IABP may offer clinical and logistical advantages over other support methods.

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