Journal of Visualized Experiments

Utilizing Percutaneous Ventricular Assist Devices in Acute Myocardial Infarction Complicated by Cardiogenic Shock

--Manuscript Draft--

Article Type:	Invited Methods Collection - JoVE Produced Video
Manuscript Number:	JoVE62110R3
Full Title:	Utilizing Percutaneous Ventricular Assist Devices in Acute Myocardial Infarction Complicated by Cardiogenic Shock
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Additional Information:	
Question	**Response**
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Title:
Utilizing Percutaneous Ventricular Assist Devices in Acute Myocardial Infarction Complicated by Cardiogenic Shock

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K**eywords:**
Mechanical Circulatory Support
Impella
Percutaneous Ventricular Assist Devices
Cardiogenic Shock
Large bore femoral access

Summary:
Percutaneous ventricular assist devices are increasingly being utilized in patients with acute myocardial infarction and cardiogenic shock. Herein, we discuss the mechanism of action and hemodynamic effects of such devices. We also review algorithms and best practices for the implantation, management and weaning of these complex devices.

Abstract
Cardiogenic shock is defined as persistent hypotension, accompanied by evidence of end organ hypo-perfusion. Percutaneous ventricular assist devices (PVADs) are used for the treatment of cardiogenic shock in an effort to improve hemodynamics. Impella is currently the most common PVAD and actively pumps blood from the left ventricle into the aorta. PVADs unload the left ventricle, increase cardiac output and improve coronary perfusion. PVADs are typically placed in the cardiac catheterization laboratory under fluoroscopic guidance via the femoral artery when feasible. In cases of severe peripheral arterial disease, PVADs can be implanted through an alternative access. In this article, we summarize the mechanism of action of PVAD and the data supporting their use in the treatment of cardiogenic shock.

Introduction

Cardiogenic shock (CS) is defined as persistent hypotension (systolic blood pressure <90 mmHg for >30 minutes, or the need for vasopressors or inotropes), end-organ hypo-perfusion (urine output <30 mL/h, cool extremities or lactate > 2 mmol/L), pulmonary congestion (pulmonary capillary wedge pressure (PCWP) ≥ 15 mmHg) and decrease cardiac performance (cardiac index $<2.2\ \frac{L}{\min \cdot m^2}$)[1, 2] due to a primary cardiac disorder. Acute myocardial infarction (AMI) is the most common cause of CS[3]. CS occurs in 5-10% of AMI and historically has been associated with significant mortality[3,4]. Mechanical circulatory support (MCS) devices such as intra-aortic balloon pump (IABP), percutaneous ventricular assist devices (PVAD), extracorporeal membrane oxygenation (ECMO) and percutaneous left atrial to aortic devices are frequently used in patients with CS[5]. Routine use of IABP has demonstrated no improvement in clinical outcomes or survival in AMI-CS[1]. Given the poor outcomes associated with AMI-CS, the difficulties in conducting trials in AMI-CS, and the negative results of IABP use in AMI-CS, clinicians are increasingly looking to other forms of MCS.

PVADs are increasingly utilized in patients with AMI-CS[6]. In this article, we will focus our discussion primarily on the Impella CP, which is the most common PVAD used currently[6]. This device utilizes an axial flow Archimedes-screw pump which actively and continuously propels blood from the left ventricle (LV) into the ascending aorta (**Figure 1**). The device is most frequently placed in the cardiac catheterization laboratory under fluoroscopic guidance via the femoral artery. Alternatively, it can be implanted through an axillary or transcaval access when necessary[7, 8].

PROTOCOL:

This protocol is the standard of care in our institution.

1. Insertion of the PVAD (e.g., Impella CP)

1.1. Obtain common femoral access over the lower half of the femoral head under fluoroscopic and ultrasound guidance using a micro-puncture needle[9,10]. Position the micro-puncture sheath and obtain an angiogram of the femoral artery to confirm appropriate arteriotomy location[11].

1.2. Insert a 6 Fr sheath in the femoral artery.

1.3. If there is concern for ilio-femoral disease, insert a pigtail catheter in the inferior portion of the abdominal aorta and perform an angiogram of the iliofemoral system to ensure there is no significant peripheral artery disease (PAD) that may preclude PVAD insertion. If there is moderate disease or calcification of the iliac arteries consider using a longer 25 cm 14 French sheath so that the tip of the sheath is in a relatively healthy segment of the abdominal aorta.

1.4. Serially dilate the arteriotomy site over a stiff .035" wire using 8, 10 and 12 Fr dilators sequentially. Then, insert the 14 Fr peel away sheath under fluoroscopic guidance, ensuring the tip advances without resistance.

1.5. Administer heparin bolus (~100 U/kg body weight) for an ACT goal of 250 to 300 s. Alternative anticoagulation include bivalirudin and argatroban.

1.6. Use a pigtail catheter to cross into the LV using a .035" J tipped wire. Remove the J wire and check an LVEDP.

1.7. Shape the tip of the exchange length 0.018" wire included in the kit and insert it into the LV so that it forms a stable curve at the LV apex.

1.8. Make sure ACT is at goal (250 to 300 s) before insertion[12,13].

1.9. Remove the pigtail catheter and insert the pump by loading the wire on the pre-assembled loading red lumen (e.g., EasyGuide) until it exits near the label.

1.10. Remove the loading red lumen by gently pulling on the label while holding the catheter.

1.11. Advance the device in small increments under fluoroscopic guidance into the LV over the 0.018" wire.

1.12. Position the pump in the LV with its inlet 4 cm below the aortic valve and make sure it is free from the mitral chordae. Being too close to the apex can cause PVCs and trigger "suction alarms". Remove the .018" wire and once removed, start the pump. Remove excess slack so the pump rests against the lesser curvature of the aorta.

1.13. Monitor the console to make sure the motor current is pulsatile and aortic waveform is displayed. If a ventricular waveform is displayed, the pump may need to be pulled back.

1.14. If the device needs to be left in situ, remove the peal-away sheath and insert the repositioning sheath pre-loaded on the device.

1.15. Check the device position on fluoroscopy and the waveforms on the console again.

1.16. Palpate (or sense with Doppler) the distal lower extremity arterial pulses including dorsalis pedis and posterior tibial prior to and after insertion of the device. Document this appropriately in the patient's medical record.

1.17. If pulses or dopplers cannot be obtained, consider taking a lower extremity angiogram using the wire re-introducing port located on the side of the device or using another access to ensure non-obstructive flow to the lower limb.

1.18. If flow is obstructed, place a reperfusion sheath prior to transferring the patient to the CCU. In patients with PAD who are at high risk for obstructive flow, strongly consider inserting the reperfusion sheath prior to placement of the 14 Fr sheath (i.e., after step 1.4 listed above).

1.19. Monitor patients treated with a PVAD in the critical care unit (CCU) by personnel trained in its use.

2. Post-procedural care

2.1. Apply sterile dressing.

2.2. Position the device at a 45° angle when entering the skin (gauze underneath the repositioning sheath can be helpful to maintain this angle). Failure to do so may result in the arteriotomy oozing, leading to formation of a hematoma. It is also helpful to place sutures with forward pressure to avoid device migration and to prevent bleeding.

NOTE: Securing the lower extremity with a knee immobilizer can also limit device migration as a reminder to patient not to bend/move the effected limb. This should not be fastened too tightly so as not to compromise circulation.

2.3. Continue to perform routine pulse checks (palpable or Doppler).

3. Positioning

3.1. Use bedside transthoracic echocardiogram to confirm appropriate device position either prior to transfer or immediately on arrival to the cardiac ICU, depending on availability of a point of care ultrasound.

3.2. Use a parasternal long axis view to assess device position. A subxyphoid view may also be used if parasternal long axis view is not obtainable. A measurement from aortic valve to the device inlet should ideally be 3-4 cm for proper positioning of the device.

3.3. Use echocardiograms to note the position of the device as it relates to the mitral valve.

3.4. When a device needs to be repositioned, turn down the device to P2, unscrew the locking mechanism on the sterile cover to advance or retract the device. One can torque as advancing or retracting if the pigtail or inlet is too close to the mitral valve.

3.5. Lock the device in the new position and document the new position.

3.6. Following this, increase the device to the desired level of support.

3.7. After increasing the level of support, reevaluate the device position as the device can jump forward when speed increases.

NOT: If the device has been pulled back across the aortic valve, repositioning is better done in the cath lab under fluoroscopy guidance.

4. Weaning

4.1. Consider weaning when vasopressors/inotropes are at low doses or completely weaned off. Hemodynamics should be continuously monitored to maintain a CPO > 0.6 W. Carefully monitor right ventricular (RV) hemodynamics with a goal to maintain right atrial pressure (RAP) <12 mmHg and pulmonary artery pulsatility index (PAPI) >1.0[14]. Also consider obtaining pH, mixed venous saturations and lactate every 2-6 hours to monitor cardiac work and end-organ perfusion.

4.2. Decrease power by 1-2 levels over 2 hours, noting CPO, PAPI, RAP, MAP and urine output. If CPO drops <0.6 W, RAP begins to increase, urine output drops > 20 mL/h or MAP <60 mmHg, increase power to previous level.

5. Removal[12]

5.1. Use vascular closure devices to close the arteriotomy access site with complete deployment of the device performed when the large bore sheath is removed[14]. Temporary endovascular balloon tamponade or "dry field closure technique" is an effective and safe way to ensure hemostasis of the large bore access site[15].

5.2. Dial down to P1 and pull back the device into the aorta followed by change to P0 and disconnect the device from the console as the catheter is pulled out of the body.

5.2.1. Note that the device should not be left across the aortic valve at P0 due to the risk of aortic regurgitation.

5.3. If considering manual hemostasis, wait until ACT <150 and hold 3 minutes of pressure per French size.

Representative Results:

Table 1 shows the safety and efficacy of PVAD implantation[35–40].

Optimizing PVAD Outcomes

PVADs are a resource-heavy intervention that requires significant experience and expertise to optimize outcomes. The following best practices should be considered:

1. Utilizing PVAD early after shock onset
2. Utilizing PVAD prior to escalating doses of vasopressors and inotropes
3. Utilizing PVAD prior to PCI
4. Utilizing invasive hemodynamics for PVAD escalation and de-escalation
5. Minimizing PVAD complications

6. Utilizing Shock Protocols

Utilizing PVAD early after shock onset

AMI-CS is caused by coronary ischemia leading to diastolic failure, increasing LV wall tension, systolic failure and systemic hypo-perfusion. If not promptly treated, CS results in lactic acidosis, end-organ failure and death[3]. It is imperative to support patients prior to the onset of refractory shock. Patients in refractory shock go on to develop systemic inflammatory response syndrome, triggering a cascade of neurohormonal changes which are difficult to reverse[3]. This was demonstrated in the cVAD registry where patients who received MCS early, with a duration of shock before PVAD initiation of <1.25 hours, had higher survival to discharge compared with those who received PVAD after 1.25 hours[16]. This was also demonstrated by Tehrani et al. who demonstrated that for patients requiring PVAD, every 1-hour delay in escalation of therapy was associated with a 9.9% increased risk of death[17]. Notably, small randomized controlled trials which compared IABP to PVADs demonstrated a superior hemodynamic effect, but not a mortality benefit[18,19].

Utilize PVAD prior to escalating doses of vasopressors and inotropes

Use of vasopressors and inotropes is typically needed in patients presenting with AMI-CS. These medications rapidly improve blood pressure and cardiac output. Unfortunately, they also increase heart rate and afterload, resulting in increasing myocardial oxygen consumption and work[20]. They are also associated with increasing arrythmogenicity and infarct size. Given these hemodynamic effects, PVADs should be considered at the time of initiation of an inotrope or vasopressor and/or when escalating their use in patients with AMI-CS. This was demonstrated in the cVAD registry where the rate of survival to discharge was inversely proportional to the amount of inotropic support used before initiation of MCS. Patients who received 0, 1, 2, 3, or 4 or more inotropes had a 68%, 45%, 35%, 35%, and 26% rate of survival to discharge, respectively (odds ratio 2.3, 95% confidence interval 0.99 to 5.32, p=0.05)[21].

Utilize PVAD pre-PCI in AMI-CS

PCI causes a transient cessation of blood flow resulting in increasing LV volume and decreasing systolic pressure. In patients with normal LV function, these physiologic changes are typically transient and quickly recover. In patients with poor LV reserve and those presenting in AMI-CS, the physiologic effects of PCI can be catastrophic. PCI can also result in micro-embolization and reperfusion injury resulting in infarct zone expansion. Early initiation of hemodynamic support prior to PCI has been shown to improve outcomes in patients with AMI-CS. The USPella registry (n=154) demonstrated survival to discharge was significantly higher in the group which received PVAD pre-PCI as compared to post-PCI (65% vs 40%, p=0.01, OR =0.37 CI 0.19-0.72)[22]. In the cVAD registry, an analysis of 287 patients demonstrated that MCS implantation before PCI was independently associated with improved survival[16]. Lastly in the IQ database, analysis of 5,571 patients demonstrated that PVAD use pre-PCI was associated with improved survival[21].

Utilizing invasive hemodynamics to PVAD management

Use of invasive hemodynamic monitoring with pulmonary artery catheters has been associated with improved outcomes in AMI-CS patients requiring PVAD. PA catheters help to guide the

effectiveness of PVAD, the need for MCS escalation, the identification of RV failure as well in aiding weaning of such devices[21]. In a retrospective cohort study of the national inpatient sample, patients with PA catheters who were admitted with AMI-CS had decreased mortality and lower in-hospital cardiac arrest[23]. Tehrani et al also demonstrated that use of a PA catheter, along with a standardized cardiogenic shock protocol, was associated with a 39% absolute increase in survival (71% vs. 32.0%; $p < 0.01$)[17]. Recent data published from the cardiogenic shock working group also demonstrated a benefit in mortality when PA catheters were used[24]. PA catheters allowed for serial monitoring of cardiac function by parameters such as cardiac power output ($\frac{CO \times MAP}{451}$), right atrial pressure and PAPI ($\frac{systolic\ pulmonary\ artery\ pressure - diastolic\ pulmonary\ artery\ pressure}{mean\ right\ atrial\ pressure}$), which are important predictors of outcomes in AMI-CS[16,25]. PAPI, like many measures of RV function, is sensitive to loading conditions, and varies by population of patient (e.g., chronic heart failure vs pulmonary hypertension vs ACS)[26]. In the future, a more specific PAPI cut off may be provided in AMI-CS versus other conditions such as chronic advanced heart failure or post LVAD or cardiac transplant implantation[26]. It is our clinical practice to use <1.0 as the cut off for consideration of right ventricular support in AMI-CS patients[27].

Figure 1: PVAD, Detailed Anatomy and Hemodynamic Effects. (**A**) Detailed anatomy of a PVAD (This figure has been modified from Abiomed). (**B**) Hemodynamic effects of PVAD. CPO: cardiac power output, O_2: oxygen, MAP: mean arterial pressure, PCWP: pulmonary capillary wedge pressure, LVEDP: left ventricular end diastolic pressure, LVEDP: left ventricular end diastolic pressure.

Figure 2: A Shock Protocol. The algorithm for the National Cardiogenic Shock Initiative. AMI: acute MI, NSTEMI: non-ST elevation myocardial infarction, STEMI: ST-elevation myocardial infarction, LVEDP: left ventricular end diastolic pressure, MAP: mean arterial pressure, CO: cardiac output, sPAP: systolic pulmonary artery pressure, dPAP: diastolic pulmonary artery pressure, RA: right atrial pressure

Table 1. Safety and Efficacy of PVAD implantation[35–40]. IABP: Intra-aortic balloon pump, pRBC: packed red blood cells, FFP: fresh-frozen plasma, LVEF: left ventricular ejection fraction.

Table 2. Complications of PVAD[15, 41]. Diagnosis and management of complications that arise from use of left-sided PVADs.

Discussion:

Minimizing the Risks and Complications of PVAD (**Table 2**)

The hemodynamic benefits of PVAD can be significantly neutralized if complications from large-bore access occur, such as major bleeding and acute limb ischemia[28,29]. It is thus essential to minimize the risk and complications of the device.

In order to decrease access site complications and reduce the number of access attempts, ultrasound and fluoroscopic guidance should be used when obtaining femoral arterial access[10,30]. Use of micropuncture allows operators to minimize trauma if the access is deemed to be at an inappropriate site[9]. Performing an aorto-iliac angiogram prior to placement of PVAD also helps in selecting the more favorable access site[15]. Vascular closure devices and endovascular balloon tamponade are effective in achieving hemostasis in patients with large-bore access and should be utilized whenever possible at the time of device removal[15, 31].

Acute limb ischemia is a catastrophic complication of PVAD use. Assessing distal pulses in the extremity is a crucial step in early detection limb ischemia. If pulses are noted to be diminished from baseline or are absent, it is imperative to restore flow prior to the patient leaving the cardiac catheterization laboratory. The ability to create an external bypass circuit for limb perfusion is thus critical[15]. Based upon a patient's vascular anatomy an external ipsilateral, an external contralateral, or an internal contralateral circuit can be created[15]. Similarly, the ability to obtain and manage an alternative access point such as an axillary artery or transcaval access is essential in patients with PAD in an effort to avoid the risk of limb ischemia[7,8].

Hemolysis can occur in patients treated with PVAD. In the EUROSHOCK registry hemolysis was present in 7.5% of patients[28]. Hemolysis can result in anemia, acute kidney injury and result in activating a systemic inflammatory response. Repositioning the PVAD device to clear the inlet from the mitral apparatus and decreasing the P level (at the cost of decreased flow) may help mitigate hemolysis.

Utilizing Shock Protocols

The aforementioned best practices led to the conceptualization and implementation of shock protocols for the treat of AMI-CS[32]. The use of these protocols has demonstrate improved survival when compared to historical controls (**Figure 2**)[14]. Quality measures such as PVAD utilization pre-PCI, door to support times, establishment of TIMI III flow in the culprit artery, utilization of right heart catheterization, the ability to wean vasopressors and inotropes and the ability to maintaining CPO > 0.6 Watts, are systemically evaluated and reported to improve outcomes within these institutions. However, while this data shows improved survival compared to prior studies, this data largely stems from single-arm registry rather than randomized controlled trials.

Limitations of the PVAD

There are several limitations to using PVADs. Severe PAD may limit implantation options, as access may occlude the vessel and lead to limb ischemia[14]. For example, if bilateral femoral disease or bypasses are present, the device may need to be placed either via the axillary artery or by transcaval access[7,8,15]. As with other ventricular assist devices, PVADs should not be used in patients with moderate to severe aortic regurgitation, as this device will worsen the aortic regurgitation rather than achieving the desired unloading of the LV[12]. Finally, for the left-sided PVADs, presence of an LV thrombus is an absolute contraindication due to the risk of stroke or other embolic events[12]. Furthermore, an Impella CP may not provide enough cardiac output, requiring upgrade to a larger PVAD or ECMO. Finally, a long-term plan should be considered for the patient – if the patient is not a candidate for advanced therapy (bridge to transplant or LVAD), then the likelihood of recovery and the duration of PVAD use should be discussed with the patient and/or family, heart failure specialist and interventionalist.

Limitations in the data

The aforementioned studies have been significantly limited in the number of patients, and in their retrospective, observational nature. Many are based on of registries, which allow for more confounding factors. There is as yet no large-scale prospective trial which demonstrates mortality benefit of the any MCS device in AMI-CS, though these studies are currently under way[33].

Future Studies

Future studies evaluating the use of PVAD in AMI-CS must come from well powered randomized control trials. These efforts are already underway. The DanGer Shock Trial will be the first adequately powered randomized controlled trial in AMI-CS and will compare standard AMI-CS practice versus standard practice with PVAD[33,34].

With increasing utilization of PVAD in AMI-CS it is important for clinicians to identify how to place, manage and wean such devices. In this article we have summarized how to place this device, step-by-step and best practices associated with improved outcomes when utilizing such devices. Formalizing these best practices based on local experience and expertise is encouraged until data from future well-powered trials is available.

Acknowledgements:

None

Disclosures:

Dr. Aditya Bharadwaj is a consultant, proctor, and member of the Speakers Bureau for Abiomed. Dr. Mir Basir is a consultant for Abbott Vascular, Abiomed, Cardiovascular System, Chiesi, Procyrion and Zoll.

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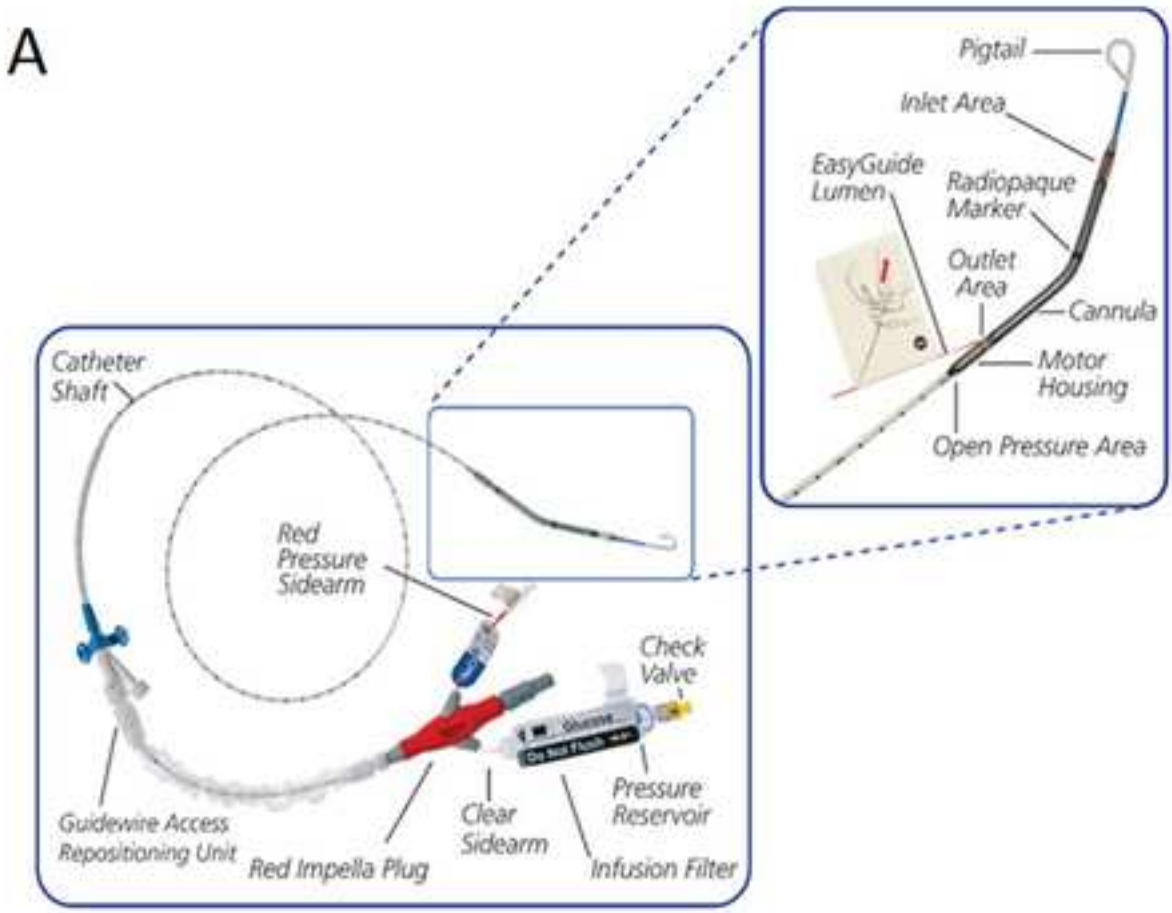
Figure 1



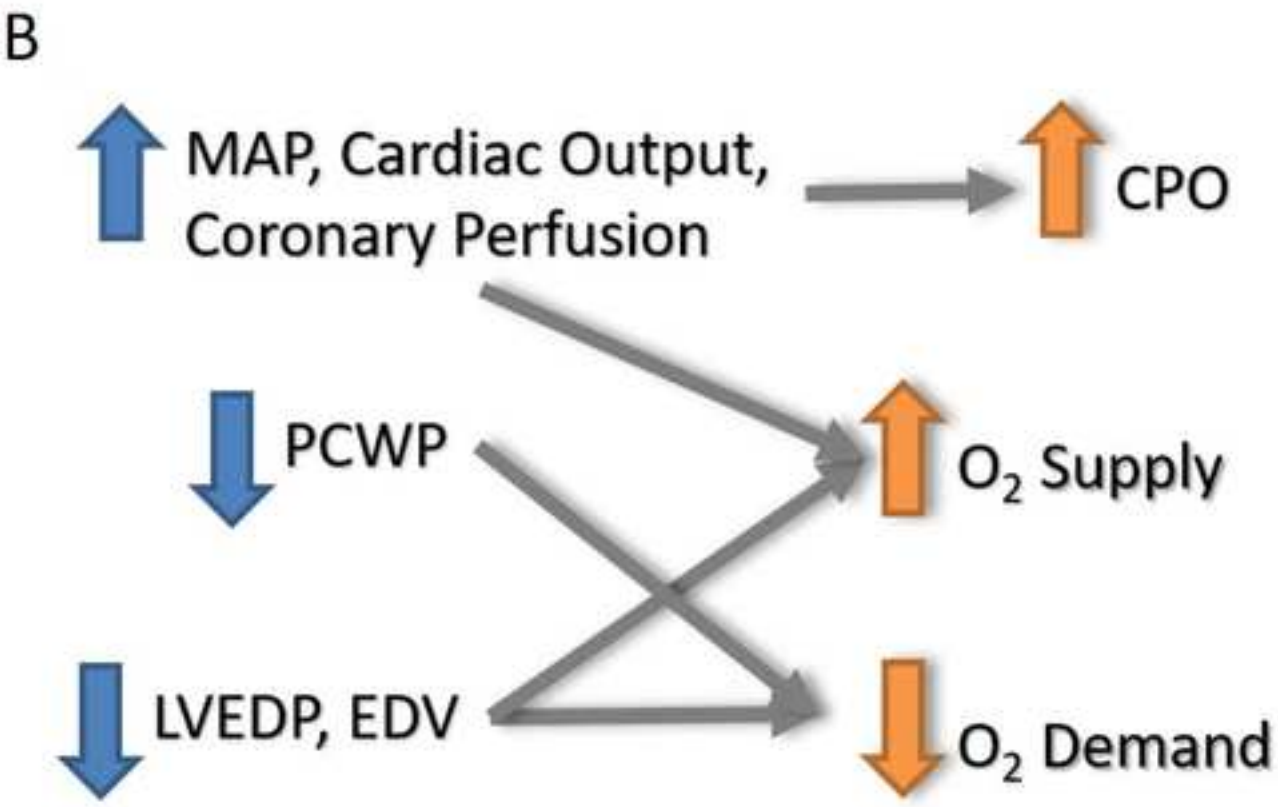


Figure 2

Click here to access/download;Figure;Figure 2 NCSI Algorithm.pdf

NATIONAL CARDIOGENIC SHOCK INITIATIVE ALGORITHM

INCLUSION CRITERIA

Acute Myocardial Infarction: STEMI or NSTEMI
- Ischemic Symptoms
- EKG and/or biomarker evidence of AMI (STEMI or NSTEMI)

Cardiogenic Shock
- Hypotension (<90/60) or the need for vasopressors or inotropes to maintain systolic blood pressure >90
- Evidence of end organ hypoperfusion (cool extremities, oliguria, lactic acidosis)

EXCLUSION CRITERIA
- Evidence of Anoxic Brain Injury
- Unwitnessed out of hospital cardiac arrest or any cardiac arrest in which ROSC is not achieved in 30 minutes
- IABP placed prior to Impella
- Septic, anaphylactic, hemorrhagic, and neurologic causes of shock
- Non-ischemic causes of shock/hypotension *(Pulmonary Embolism, Pneumothorax, Myocarditis, Tamponade, etc.)*
- Active Bleeding
- Recent major surgery
- Mechanical Complications of AMI
- Known left ventricular thrombus
- Patient who did not receive revascularization
- Contraindication to intravenous systemic anticoagulation
- Mechanical aortic valve

ACTIVATE CATH LAB

ACCESS & HEMODYNAMIC SUPPORT
- Obtain femoral arterial access (via direct visualization with use of ultrasound and fluoro)
- Obtain venous access (Femoral or Internal Jugular)
- Obtain either Fick calculated cardiac index or LVEDP

IF LVEDP >15 *or* Cardiac Index < 2.2 AND anatomy suitable, place IMPELLA

Coronary Angiography & PCI
- Attempt to provide TIMI III flow in all major epicardial vessels other than CTO
- If unable to obtain TIMI III flow, consider administration of intra-coronary vasodilators

Perform Post-PCI Hemodynamic Calculations

1. Cardiac Power Output (CPO): $\frac{MAP \times CO}{451}$

2. Pulmonary Artery Pulsatility Index (PAPI): $\frac{sPAP - dPAP}{RA}$

** QUALITY MEASURES **
- Impella Pre-PCI
- Door to Support Time < 90 minutes
- Establish TIMI III Flow
- Right Heart Cath
- Wean off Vasopressors & Inotropes
- Maintain CPO >0.6 Watts
- Improve survival to discharge to >80%

Wean OFF Vasopressors and Inotropes
If CPO is >0.6 and PAPI >0.9, operators should wean vasopressors and inotropes and determine if Impella can be weaned and removed in the Cath Lab or left in place with transfer to ICU.

Escalation of Support
If CPO remains <0.6 operators should consider the following options:
- PAPI is <0.9 consider right sided hemodynamic support
- PAPI >0.9 consideration for additional hemodynamic support

Local practice patterns should dictate the next steps:
- Placement of more robust MCS device(s)
- Transfer to LVAD/Transplant center

If CPO is >0.6 and PAPI <0.9 consider providing right sided hemodynamic support if clinical suspicion for RV dysfunction/failure

Vascular Assessment
- Prior to discharge from the Cath Lab, a detailed vascular exam should be performed including femoral angiogram and Doppler assessment of the affected limb.
- If indicated, external bypass should be performed.

ICU Care
- Daily hemodynamic assessments should be performed, including detailed vascular assessment
- Monitor for signs of hemolysis and adjust Impella position as indicated

Device Weaning
Impella should only be considered for explantation once the following criteria are met:
- Weaning off from all inotropes and vasopressors
- CPO >0.6, and PAPI > 0.9

Bridge to Decision
Patients who do not regain myocardial recovery within 3-5 days, as clinically indicated, should be transferred to an LVAD/Transplant center. If patients are not candidates, palliative care options should be considered.

NATIONAL CARDIOGENIC SHOCK INITIATIVE

NationalCSI@hfhs.org

www.henryford.com/cardiogenicshock

Study	Patient Population	N
Seyfarth et al	Acute myocardial infarction and Cardiogenic Shock	25
Schrage et al.	Acute myocardial infarction and Cardiogenic Shock	237
Casassus et al.	Refractory cardiogenic shock from acute myocardial infartion	22
Joseph et al.	Acute myocardial infarction and cardiogenic shock	180
Lauten et al.	Acute Myocardial Infarction and Cardiogenic Shock	120
Ouweneel et al	Acute myocardial infarction and cardiogenic shock	48

Devices Compared	Findings
IABP vs Impella 2.5	No device-related technical failure Non-statistically significant ↑pRBC transfusion in Impella group Non-statistically significant ↑FFP in Impella Group ↑Hemolysis in Impella group No difference in mortality or LVEF
IABP vs Impella CP and 2.5	No difference in Mortality, Stroke ↑Bleeding and ischemic complications inImpella group compared to IABP group
Impella 2.5	Transfusion due to bleeding: 18.2% limb ischemia: 10% aortic insufficiency: 5.6%
Impella 2.5	Hemolysis: 8.9% No aortic regurgitation Bleeding requiring transfusion: 15.6% Vascular complication: 11.7%
Impella 2.5	Major Bleeding 28.6% Hemolysis: 7.5%
IABP vs Impella CP	Hemolysis: 8% No incidence of device failure Device-related bleeding: 13% Major Vascular complication: 4% No significant difference in mortality

Complication	Diagnosis
Acute Limb Ischemia	• Clinical: Decreased or absent pulses on limb, limb pain, change in color to pale, blue. • Imaging: Minimal or no pulse via Doppler ultrasound. • Laboratory: elevation in lactate
Vascular Pseudoaneurysm	• Clinical: large, pulsatile mass, painful at access site, +thrill/bruit • Imaging: Doppler Ultrasound
Bleeding (external hematoma or internal retroperitoneal bleed)	• Clinical: hypotension despite improved cardiac output, visible hematoma, suction alarms • Laboratory: ↓hemoglobin • Imaging: CT scan without contrast to diagnose retroperitoneal bleed
Hemolysis	• Clinical: change in color of urine to dark yellow, brown. • Laboratory: ↑ plasma-free hemoglobin, lactate dehydrogenase, bilirubin. ↓ hemoglobin, haptoglobin.

Management	Prevention
• Internal or External percutaneous bypass, restoring antegrade flow • Removal of Impella device, re-insertion at another arterial site with less vascular disease if needed for hemodynamic support	• Routine assessment of distal pulses • If distal pulse is compromised, recommend creation of external or internal bypass to restore flow
• <2-3cm, may resolve spontaneously • Ultrasound-guided thrombin injection • Surgical intervention (rapid increase in size, peripheral neuropathy, distal/cutaneous ischemia)	• Meticulous access techniques including use of Ultrasound, Fluoroscopy and micro-puncture access
• If hematoma or oozing around access site, reposition angle of Impella • Low-pressure balloon inflation at site of bleeding or covered stent deployment in extreme cases • Coil embolization for retroperitoneal bleed	• Meticulous access technique with Ultrasound, Fluoroscopy and micro-puncture sheath to prevent 'high stick' (prevents retroperitoneal bleed) and minimize access attempts (prevents hematoma)
• Reposition device, generally away from mitral leaflet • Decrease power level • Removal of device if requiring significant blood transfusions (> 2 units) or causing renal function compromise.	• Good Impella position with inlet away from mitral apparatus

Table of Materials

Name of Material/ Equipment	Company	Catalog Number	Comments/Description
4 Fr-018-10 cm Silhouette Stiffened Micropuncture Set	Cook	G48002	Microvascular access
5 Fr Infiniti Pigtail Catheter	Cordis	524-550S	pigtail catheter
Impella CP Intra-cardiac Assist Catheter	ABIOMED	0048-0003	Impella catheter kit

Revision 3 Rebuttal:

Reviewer's Comments:

Reviewer #2:
Manuscript Summary:
Thank you for revising the manuscript.

Minor Concerns:
Limitations of the PVAD
- Comment on aortic regurgitation repeated

Thank you for noting this. We have removed one of the statements.

- Should include inadequate hemodynamic support as a limitation of Impella CP

We have included this statement in lines 300-301.

Reviewer #4:
This is a nice overview on Impella placement and best practices. I still would like to see the authors clearly state that despite the use of shock protocols that have demonstrated improved survival when compared to historical controls as stated in their discussion, the data has not been generated from RCTs and only based on centers retrospective and prospective review of data. When Impella use in CS is looked at in a randomized clinical trial, the data show superior hemodynamic benefit compared to IABP BUT no survival benefit.
This needs to be clearly stated.

Thank you for this feedback, we have addressed this in lines 204-205 and lines 288-290.

From: Langford, Tom
Sent: Tuesday, January 19, 2021 6:31 AM
To: Shuktika Nandkeolyar; Aditya Bharadwaj
Subject: RE: <EXT> Permission from Abiomed to use figures

Hi Shuktika,

Happy to help.

Abiomed officially grants you and JOVE permission to publish the images of Impella CP provided to you by Mary McLoughlin in September.

Let me know if anything else is needed.

Tom

Tom Langford
Director of Communication

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978-882-8408 Office
617-771-4510 Mobile
tlangford@abiomed.com
www.abiomed.com

Recovering hearts. Saving lives.

From: Shuktika Nandkeolyar <shuktikan@gmail.com>
Sent: Tuesday, January 19, 2021 12:17 AM
To: Aditya Bharadwaj <adityadoc@gmail.com>; Langford, Tom <tlangford@abiomed.com>
Subject: Re: <EXT> Permission from Abiomed to use figures

Dear Tom,

My name is Shuktika Nandkeolyar, and I am a cardiology fellow working with Dr. Aditya Bharadwaj on a manuscript on Impella use in cardiogenic shock for JOVE. We need an official "permission to use" email with regards to figures of the Impella CP (we had been provided these figures by Mary McLoughlin earlier in September), and you had mentioned you'd be able to arrange this for us (thread is below for context). Please let me know if there is anything else I would need to do to facilitate this.

Thanks,

Shuktika

> Begin forwarded message:

From: Aditya Bharadwaj <adityadoc@gmail.com>
Date: September 17, 2020 at 10:33:33 PM PDT
To: "McLoughlin, Mary" <mmcloughlin@abiomed.com>
Subject: Re: <EXT> Permission from Abiomed to use figures

Thank you so much for this information!

Aditya

> On Sep 17, 2020, at 9:50 AM, McLoughlin, Mary <mmcloughlin@abiomed.com> wrote:
>
> FYI
> Mary M. McLoughlin
> ABIOMED, Inc.
> 978-289-3684
>
> **From:** Langford, Tom <tlangford@abiomed.com>
> **Sent:** Thursday, September 17, 2020 12:37:39 PM
> **To:** McLoughlin, Mary <mmcloughlin@abiomed.com>; Garcia Palmer, Lillian <lpalmer@abiomed.com>
> **Subject:** RE: <EXT> Permission from Abiomed to use figures
>
> Hi Mary,
>
> The publisher will likely need a formal “permission granted” email from us.
>
> Let him know if he needs to formally obtain permission, he can email me and Sarah Karr and we will take care of it.
>
> Thanks!
>
> **Tom Langford**
> Director of Communication
>
> **ABIOMED, Inc.**
> 22 Cherry Hill Drive | Danvers, MA 01923
> 978-882-8408 Office
> 617-771-4510 Mobile
> tlangford@abiomed.com
> www.abiomed.com
>
> **Recovering hearts. Saving lives.**

> **From:** McLoughlin, Mary <mmcloughlin@abiomed.com>

Sent: Thursday, September 17, 2020 7:11 AM
To: Langford, Tom <tlangford@abiomed.com>; Garcia Palmer, Lillian <lpalmer@abiomed.com>
Subject: Fwd: <EXT> Permission from Abiomed to use figures

Tom I sent aditya the media link from website too. Does he need any permissions to use images?

Mary M. McLoughlin
ABIOMED, Inc.
978-289-3684

From: Aditya Bharadwaj <adityadoc@gmail.com>
Sent: Thursday, September 17, 2020 2:16:11 AM
To: Garcia Palmer, Lillian <lpalmer@abiomed.com>
Cc: McLoughlin, Mary <mmcloughlin@abiomed.com>
Subject: <EXT> Permission from Abiomed to use figures

Hi Lillian and Mary,

I am working on a manuscript for a journal on Best Practices for Impella use in Cardiogenic shock. We would like to use the figures that I have attached. We will give credit to Abiomed in the footnote of the figure. In addition, do we have to obtain permission by filling out a form?

Thanks,
Aditya

--
Shuktika Nandkeolyar