Review

The role of mechanical support devices during percutaneous coronary intervention

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Abstract

The practice of interventional cardiology has changed dramatically over the last four decades since Andreas Gruentzig carried out the first balloon angioplasty. The obvious technological improvements in stent design and interventional techniques have facilitated the routine treatment of a higher risk cohort of patients, including those with complex coronary artery disease and poor left ventricular function, and more often in the setting of cardiogenic shock (CS) complicating acute myocardial infarction (AMI). The use of mechanical cardiac support (MCS) in these settings has been the subject of intense interest, particularly over the past decade . A number of commercially available devices now add to the interventional cardiologist's armamentarium when faced with the critically unwell or high-risk patient in the cardiac catheter laboratory. The theoretical advantage of such devices in these settings is clear- an increase in cardiac output and hence mean arterial pressure, with variable effects on coronary blood flow. In doing so, they have the potential to prevent the downward cascade of ischaemia and hypoperfusion, but there is a paucity of evidence to support their routine use in any patient subset, even those presenting with cardiogenic shock. This review will discuss the use and haemodynamic effect of MCS devices during percutaneous coronary intervention (PCI), and also examine the clinical evidence for their use in patients with cardiogenic shock, and those undergoing 'high risk' PCI

Keywords

PCI, IABP, ECMO, CS, high risk patient

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Introduction

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use in patients with cardiogenic shock, and those undergoing 'high risk' PCI.

Theoretical principles of mechanical support

In severe LV systolic dysfunction, myocardial contractility and stroke volume are reduced whilst LV end diastolic volume/pressure (LVEDV/P) is increased leading to decreased cardiac output (CO) and end organ hypoperfusion. In normal physiological circumstance stroke volume/work and myocardial oxygen demand are determined by preload, myocardial contractility and afterload. At cardiac level preload is most often taken to be LVEDP or LAP (Left atrial pressure) while after load is wall stress, in turn defined as LV pressure × cavity radius/wall thickness.[8]

In CS complicating AMI the left ventricle (LV) is unable to effectively unload leading to an increased LVEDP, low CO, increased wall stress and stroke work, decreased myocardial perfusion, end organ perfusion and increased myocardial oxygen demand thus creating a downward spiral of haemodynamic compromise, systemic inflammatory response and worsening myocardial ischaemia.[9] Though many clinical factors (age at presentation, time to reperfusion, infarct size, delayed presentation, out of hospital cardiac arrest, adequacy of revascularisation) are associated with outcomes in AMI, multiple studies have identified the haemodynamic parameter of cardiac power output (CPO) defined ascardiac output x mean arterial pressure/451, <0.6 watt to be an important predictor for in hospital mortality in patients admitted with CS[8,10,11]

In patients with a large ischaemic burden and poor LV function undergoing PCI, further ischaemia can lead to a further reduction in contractility of an already depressed ventricle and trigger a circulatory collapse. Therefore, MCS has the potential haemodynamic effect of unloading the LV, decreasing LVEDP/LVEDV, stroke work, increasing cardiac output and thereby improving systemic and coronary perfusion.

Available percutaneous support devices

Currently available percutaneous MCS devices are shown in Figure 1, with a comparison of their mechanism, haemodynamics and procedural aspects of implantation in Table 1. The ideal MCS device is able to provide haemodynamic support to maintain adequate systemic perfusion, improve mean arterial pressure, and decrease myocardial oxygen demand by a concomitant reduction in left ventricular pre and after load, whilst maintaining, or increasing coronary perfusion.

The intra-aortic balloon pump (IABP)

The intra-aortic balloon pump (IABP) was introduced into clinical practice in 1968 and remains the most widely used percutaneous MCS, due to availability and ease of insertion.[12] The device is usually inserted via the femoral artery, although the axillary, brachial and iliac routes have also been successfully used. The distal end of device is positioned retrogradely, 2–3 cm distal to left subclavian artery at the level of carina. Balloon inflation is with helium, used due to its low viscosity that facilitates easy transfer in and out of the balloon in addition to its rapid absorption in blood in case of balloon rupture. The IABP counter pulsation mechanism is triggered by invasive arterial pressure or the electrocardiogram. The balloon is fully inflated at onset of diastole after closure of the aortic valve with deflation before opening. Given that most coronary blood flow occurs in diastole, counterpulsation therefore augments coronary perfusion when microcirculatory autoregulation has been exhausted in stenosed coronary arteries as well as reducing afterload and cardiac work.[13]

The device is simple to use and has a very low profile compared to other devices, but the degree of

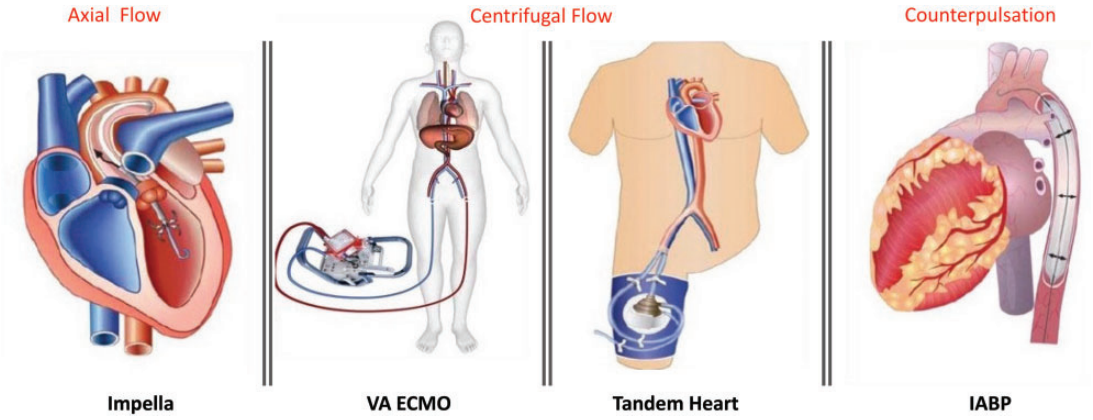

Figure 1. Percutaneous LV support options available.

Table 1. Comparison of different mechanical support devices.

	IABP	IMPELLA	Tandem Heart	VA ECMO
Mechanism				
Principle	Pneumatic (pressure counterpulsation)	Axial flow	Centrifugal flow	Centrifugal flow
Cardiac synchrony	Yes	No	No	No
Haemodynamics				
Flow rate	0.3–0.5L/min	1–5L/min	2.5–5 L/min	3–7L/min
Cardiac power output	↑	↑↑	↑↑	↑↑
LV preload	—	↓↓ [a]	↓↓	↓↓
LVEDP	↓	↓↓	↓↓	↔
Afterload	↓	↓	↑	↑↑↑
PCWP	↓	↓↓	↓↓	↔
Coronary perfusion	↑	?	?	?
Myocardium O2 demand	↓	↓	↓↔	↔
TPR	↓	↓	↑	↑↑
Haemodynamic support	+	++	+++	+++
Procedural aspects				
Sheath size	7–8 Fr	13–14 Fr , Impella 5.0–21 Fr	15–17 Fr Arterial 21 Fr Venous	14–16 Fr Arterial 18-21 Fr Venous
Implantation time	Short	Short - Medium	Long	Medium
Maximum no. of implant days	≥7 Days	7 Days	14 Days	Weeks
Closure	Percutaneous	Percutaneous/ Surgical	Surgical	Surgical
Cost	£400-600	£6600–15000	£90,000[b]	£10,000

IABP: intra aortic balloon pump; VA ECMO: venoarterial extracorporeal membrane oxygenation; LV: left ventricle; LVEDP: left ventricle end diastolic pressure; PCWP: pulmonary capillary wedge pressure; O2: oxygen; TPR:total peripheral resistance; Fr:French; L/min liters/min.
[a]Impella is dependent on preload for effective action? = Unknown (Reference: 57).
[b]Incremental cost effectiveness ratio (ICER).

haemodynamic support generated is modest. The precise augmentation of cardiac output will vary, and requires cardiac synchrony, optimal balloon position, sizing and timing of balloon inflation in diastole and deflation in systole. The MEGA IABP (50 cc balloon) can provide a greater haemodynamic support compared to a standard size IABP with no increase in vascular complication rate.[14,15] The IABP can be used without a need for anticoagulation if risk of bleeding is high with no increment in rate of limb ischaemia or thromboembolism.[16] Severe aortic regurgitation (AR) is an absolute contraindication to use of device and caution should be taken when inserting device in patients with severe peripheral arterial disease.[7,17] Other relative contraindications and complications associated with device use are summarised in Table 2.

The impella

The Impella device (Abiomed, Danvers, Massachusetts) is catheter based miniaturised rotatory blood pump, usually inserted percutaneously through a 13–14 French sheath, with larger devices implanted via a surgical cut down. Given the size of the device, careful planning is required to ensure that the peripheral vessels are of adequate calibre. Whilst it is typically inserted via the transfemoral route, the axillary and transcaval approaches have also been used.[18] The device, mounted on a 9 Fr Pigtail, is advanced retrogradely to the left ventricular cavity and is placed across the aortic valve. The distal end of catheter is connected to a portable mobile console that displays true invasive pressure, revolutions per minute of the pump and guides the correct positioning of the device. The micro axial pump continuously aspirates blood from the LV and expels it into the ascending aorta at rates of 2.5–5 liters/min (L/min). This leads to a reduction in LV volume with a concomitant increase in mean aortic pressure. As a result, systemic perfusion is increased, LV wall stress is reduced, and the transmyocardial perfusion gradient (aortic diastolic pressure – LV diastolic pressure) is increased. The effect on coronary haemodynamics is less well understood, but the device does appear to increase coronary perfusion pressure.[19] Unlike the IABP, the Impella is independent of LV function and does not require cardiac synchrony.[20] The effect of the Impella device on all parameters of cardiac function are far greater than the IABP, and indeed these effects are enhanced with the larger devices. Three versions of the Impella device are currently available: the Impella LP 2.5 (2.5 L flow), the lmpella CP (3.7 L flow),

Table 2. Contraindications and risks associated with MCS.

	IABP	Impella	Tandem Heart	VA ECMO
Contraindication				
Vascular	Severe PAD	Severe PAD	Severe PAD	Severe PAD
Valve	Mod-Severe AR	Mechanical Aortic Valve, Mod-Severe AR, AS with AVA $< 0.6cm^2$	Severe AR	Mod-Severe AR
Structural	Significant Aortic Disease i.e. aortic aneurysm/ dissection	LV thrombus	LA thrombus, VSD	Unrepaired aortic dissection
Complication				
Bleeding	Low	Moderate	Very High	High - Very High
Vascular	Low	Moderate- High	High	Very High
Haemolysis	No	Yes	Yes	Yes
Device related	Balloon Rupture	Device Migration/Malfunction	Device Migration	Device Malfunction
Rare	Aortic Dissection/Rupture, Thrombocytopenia	Aortic Valve Injury	Cardiac Tamponade	Thrombocytopenia, Neurological Injury

PAD: peripheral arterial disease; AR: aortic regurgitation; AS : aortic stenosis; AVA: aortic valve area; LV: left ventricle; LA: left atrium; VSD : ventricular septal defect.

both of which can be implanted percutaneously, and the Impella LP 5 (5 L flow) which requires a surgical cut down. Despite increased operator experience and improvement in technology, device related haemolysis, bleeding and vascular complication rate remain high in recent registries and potentially blunt the haemodynamic gains from the device[21–23] A careful assessment of the peripheral vasculature is recommended to minimise the vascular complication risk, and implantation should ideally be ultrasound guided. Haemostasis at the arteriotomy site is routinely achieved with vascular closure devices (VCD).[24] Absolute contraindications to device use include LV thrombus, severe aortic regurgitation and contraindication to use of anticoagulation.[7,17]

More recently, an Impella device has been developed for right ventricular failure. The RP is a 22 Fr catheter based microaxial pump available for refractory right ventricular (RV) failure and is inserted via a femoral vein percutaneously; pump inflow is placed in inferior vena cava and outflow in pulmonary artery. The device can achieve an augmented forward flow of >4 L/min in pulmonary artery, reducing RV load and thereby increasing cardiac index. The safety and efficacy of device has been reported in very small series to date, demonstrating improved haemodynamics in patients with refractory right ventricular failure.[25,26] In acute biventricular failure Impella 2.5/5.0/CP and Impella RP can be used together- Bipella, to provide haemodynamic support, facilitate LV/RV unloading and augment coronary and systemic perfusion.[27]

The tandem heart

The Tandem Heart is an extracorporeal, centrifugal continuous flow device that can be used for left, right or biventricular failure. A 21 Fr transseptal cannula withdraws oxygenated blood from left atrium (LA) and is pumped back to iliofemoral arterial system using a 15 Fr–19 Fr arterial cannula using a centrifugal pump, thereby bypassing the LV. The pump can provide flows of 2.5–5 L/min[28]

By aspirating blood from LA, the system significantly reduces LV preload, filling pressures, and myocardial oxygen demand, whilst cardiac output and mean arterial pressure are augmented as blood is propelled back into arterial system. If retrograde flow from device exceeds forward flow from the LV this can result in aortic valve closure and there is a theoretical need to 'vent' the left ventricle. Anticoagulation is required with an activated clotting time (ACT) of 250–300 seconds recommended prior to device activation.

The size of the device, and the need for a transseptal puncture has limited its use. A major drawback remains the high incidence of vascular complications, device migration and cardiac tamponade. In a small randomised trial, Thiele et al. compared the use of the Tandem Heart with the IABP in patients with cardiogenic shock. Although clearly underpowered, no difference in outcome was seen between the two groups, but a much higher rate of major vascular complications and need for blood transfusion was associated with Tandem Heart.[29]

The device has limited availability in National Health Service (NHS) and has a high estimated incremental cost effectiveness ratio (ICER) at £90,000[30] (Table 1).

Venoarterial extra corporeal membrane oxygenation (VA ECMO)

VA ECMO is a form of heart-lung bypass which offers temporary mechanical support and simultaneous

extracorporeal gas exchange in patients with refractory cardiogenic shock, usually acting as a bridge to recovery or destination therapies. It has been used widely since its introduction in 1972. VA ECMO can be implanted via a surgical cut-down in the operating theatre via sternotomy, surgical cannulation of right atrium and aorta- Central ECMO but is more routinely implanted percutaneously via a transfemoral/trans axillary approach- Peripheral ECMO. An 18–21 Fr cannula is inserted via femoral vein to right atrium and deoxygenated venous blood is withdrawn. The blood is then pumped through a membrane oxygenator in an extracorporeal centrifugal pump, oxygenated blood is returned to femoral artery through a 14–16 Fr reinfusion cannula. VA ECMO results in a dramatic increase in cardiac output and mean arterial pressure (Figure 1) and will usually achieve an increased flow rate of 4–6 L/minute.

Peripheral ECMO is a retrograde arterial system and can dramatically increase afterload leading to a higher LVEDP and increased myocardial oxygen demand. In CS setting if afterload generated by ECMO exceeds LVEDP, an already depressed LV cannot generate enough power to unload and the aortic valve remains closed for entire cardiac cycle which leads to LV distension, further increasing LVEDP and pulmonary capillary wedge pressure (PCWP) precipitating pulmonary oedema and acute lung injury. Further, stagnant blood is a nidus for thrombus formation in the LV cavity and aortic root with the consequent risk of thromboembolic complications.

The risk of LV distension with ECMO can be mitigated by venting the LV, either by increasing forward flow with use of inotropes/Impella, decreasing afterload by placement of an IABP, or direct decompression with an atrial septostomy. This can also be facilitated by decreasing intravascular volume with haemodialysis/diuretics or reducing the flow rate.[31,32]

There has been a significant improvement in device technology and increased operator experience, however the technology is still associated with a risk of significant complications, particularly related to the vascular access site- specially limb ischaemia associated with peripheral ECMO which can be mitigated with a reperfusion circuit established distal to the main arterial access site to maintain distal limb perfusion. Bleeding and haemolysis are also higher compared to other MCS due to blood loss in device, acquired von Willebrand syndrome, thrombocytopenia, and fragmentation of red cells due to high shear stress and mechanical strain (Table 2).[7,17,33]

Mechanical circulatory support in cardiogenic shock

Cardiogenic shock is defined by a combination of persistent hypotension (systolic blood pressure <80–90 mm Hg or mean arterial pressure 30 mm Hg lower than baseline), cardiac index (CI) <1.8 L/min/m^2 without support or <2.0–2.2 L/min/m^2 with support, elevated filling pressures (LVEDP > 18 mm Hg or RVEDP > 10–15 mmHg), as well as clinical signs/symptoms of hypoperfusion (cool extremities, decreased urine output, high lactate or altered mental status).[5] CS complicates 6% to 8% of patients with acute myocardial infarction (AMI). Despite advances in PCI technique, availability of MCS and improved supportive care, the mortality of CS has remained static over the past 20 years.[34,35] Whilst early and appropriate revascularisation of the culprit vessel in this setting improves survival, the evidence for mechanical support is much more limited..[34–37]

Clearly CS leads to reduced myocardial contractility and stroke volume, with concomitant increase in LVEDV, LVEDP and myocardial oxygen demand. Though there are clear theoretical benefits associated with the use of MCS devices in CS and often impressive effects on haemodynamic parameters, no study to date has shown that the use of MCS leads to an improvement in clinical outcome.[29,38–41] This is a difficult patient population to include in randomised trials, for obvious reasons, and numerous questions remain regarding the timing of mechanical support, in particular whether this should take place before, during or after revascularisation, the intensity of other supportive therapies and patient selection.

The IABP is the most widely studied device in patients presenting with cardiogenic shock, which is not surprising given the ease of use, widespread availability and low cost. An early non-randomised study suggested improved survival with IABP use in 90 patients treated at two centres.[42] The TACTICS study was a small single centre randomised trial which compared use of IABP in AMI with standard therapy. The study recruited only 47 patients, was therefore distinctly underpowered, and showed no difference in outcome between the two groups at 6 months.

Despite the limited data the routine use of IABP was encouraged by international guidelines receiving a Class I recommendation for much of the past 3 decades. Indeed, in the SHOCK study almost 90% of patients received an IABP whether or not they received urgent revascularisation.[34]

The IABP SHOCK I was a small sample randomised trial that investigated haemodynamic benefit and survival improvement with use of IABP in addition to PCI in CS complicating AMI. Although there was an initial improvement in haemodynamic parameters, beneficial effects were not sustained after 24 hours.[43] The IABP in Cardiogenic Shock (IABP SHOCK- II) is the only large-scale randomised trial examining the use of an MCS in AMI. In this study 600 patients with

CS complicating AMI were randomised to IABP versus no IABP, with 80% of included patients receiving the device after PCI. 10% of the control group had IABP implantation within the first 24 hours There was no difference in mortality between the two groups at 30 days, and this was sustained at 5 year follow up, in both the intention to treat, and as-treated cohorts.[44,45] Importantly, there was no major difference in heart rate or blood pressure between the two groups, and indirect markers of end-organ perfusion such as serum lactate and renal function did not differ. Placement of the IABP before revascularisation had no apparent effect, although the numbers were too small to draw firm conclusions. There are numerous possible reasons why the IABP SHOCK II study was neutral. Augmentation of CO to maintain end organ transfusion was minimal and residual ischaemia from untreated bystander coronary artery disease may have affected long term outcomes.

Given the difficulties in performing randomised trials in this patient cohort, observational data is of interest. Several early registries suggested a mortality benefit of the IABP use following thrombolysis in CS complicating AMI[46,47] however this has not been seen in metanalyses from the PCI era.[48–50]

The results from the IABP-SHOCK II study have had an inevitable impact on clinical guideline recommendations. The *routine* use of the IABP in CS has been downgraded from Class I to a Class III (not recommended) in the European guidelines.[51] The change in guidelines has led to a concomitant reduction in IABP use across the US and Europe, as evidenced by several recent registries.[2]

Other MCS devices have been less widely studied in both CS and high-risk PCI. The Impella device was the focus of one small, randomised multicentre study, the IMPRESS trial. 48 mechanically ventilated patients with CS were randomised 1:1 to IABP or the Impella device. 30 day and 6-month mortality were identical between the two groups (50% Impella vs 46% IABP) but the trial was not powered for any meaningful clinical end-points.[41] As expected, the more powerful device delivered an impressive increase in haemodynamic parameters, with amelioration of mean arterial pressure, a reduction in ionotropic requirements and lower lactate in the first 24 hours, however there were more bleeding event in Impella cohort. There are a number of limitations of this study, not least the small numbers recruited. The less powerful 2.51 LP device was used, randomisation occurred after revascularisation, and a larger number in the Impella group received the device upfront 21 vs 13% in IABP group.[41]

Seyfarth et al. in the ISAR Shock trial explored safety and haemodynamic effect of Impella LP 2.5 compared to IABP in patients with CS complicating AMI.[40] There was an increase in Cardiac index in the Impella group and early reversal of serum lactate levels within 30 min of device implantation, however the Impella group required more blood transfusion. There are several limitations to the study ,it was not adequately powered for clinical endpoints, CI was measured for a short period of time and device was implanted post revascularisation.[52]

Karatolios et al. examined the use of the Impella in a single centre, retrospective cohort including only 20 patients.[53] In this study the Impella group had a more prolonged low flow time period, higher serum lactate and worse LV function on admission.The device was associated with improved survival at discharge and 6 months after propensity score matching.[53]

Schrage et al. matched 237 patients from IABP SHOCK II trial with 237 treated with Impella LP 2.5/CP for CS complicating AMI from EUROSHOCK registry and found no reduction in 30 day mortality with Impella use compared to IABP/ standard medical therapy.[54]

A subsequent meta-analysis showed a higher vascular and bleeding complications with no difference in outcome with Impella use.[55]

Thiele et al. compared IABP with percutaneous LV assist device (Tandem Heart) in patients with CS complicating AMI. 41 patients, all mechanically ventilated were randomly assigned (1:1) , VAD Tandem heart significantly improved cardiac power index (CPI) and effectively lowered serum lactate compared to IABP, but was associated with a significantly higher rate of vascular and bleeding complications with no difference in 30-day mortality between groups (45% vs 43%).[29]

Evidence for ECMO in CS is limited and data for clinical use is from non-randomised trials and large-scale registries. ECMO is associated with improved short term survival and favourable neurological outcome in patients with out of hospital cardiac arrest and CS complicating AMI.[56,57]

MCS during high risk PCI

PCI has evolved significantly over the four decades since its development. Technological improvements include improved stent, balloon and delivery systems. Advanced imaging, adjunctive technology and a smorgasbord of complex interventional techniques have allowed the interventional cardiologist to deal with lesions of increasing complexity.

There are a number of factors which increase procedure complexity. Patient demographics such as advanced age, and baseline left ventricular function, must be considered in combination with the coronary anatomy in order to assess risk .The term 'high risk PCI' has been coined to encompass treatment for this patient group with complex coronary anatomy and poor LV systolic

function who have indications for coronary revascularisation, but are at high procedural risk[7,58]

There is currently no uniform definition of high-risk PCI. However, there are a number of variables that potentially increase procedural complications and can be broadly grouped into the following: patient comorbidities/presentation, LV function/valvular disease and complexity of the coronary anatomy (Figure 2). In patients with a large ischaemic burden and poor LV systolic function, sustained hypotension with reduced coronary perfusion during PCI can lead to profound myocardial ischaemia, and further insult to an already impaired LV, with the potential to cause circulatory collapse and arrest.[7]

MCS can theoretically prevent this spiral by providing haemodynamic stability throughout the procedure, increasing cardiac output to maintain myocardial and systemic perfusion, decrease myocardial oxygen demand and improve coronary perfusion.[8]

However, despite the sound theoretical basis for the use of MCS during high risk PCI, there is a distinct paucity of evidence to support its use, with a limited number of randomised trials and observational studies[59,60]

The Balloon pump–assisted Coronary Intervention Study (BCIS-1) was a randomised, multi-center study which investigated whether elective use of IABP in high risk PCI reduced major adverse cardiovascular and cerebrovascular events (MACCE) at 28 days. 301 patients with severe LV impairment and severe coronary artery disease (BCIS -1 jeopardy score >8) were randomised to receive PCI with or without IABP (150). The elective use of the IABP use had no effect on MACCE at 28 days although baseline demographics were similar, and procedural success was >90%. There was a higher procedural complication rate in the 'unplanned' IABP group (10.7% vs 1.3%, $P < 0.001$). The degree of revascularisation was similar in both groups. Interestingly, at 51 months follow up there was a 34% relative reduction in all-cause mortality in IABP group.[61] This apparent benefit at long term follow up may be a chance finding, and little to support a mechanistic benefit for this difference between the groups.

The Intra-aortic Balloon Counterpulsation and Infarct size in patients with Acute Anterior Myocardial Infarction Without Shock (CRISP AMI) was a randomised, multicenter study which explored whether implantation of IABP prior to undertaking primary PCI in patients with anterior STEMI without CS reduces infarct size, measured by cardiac magnetic resonance imaging (CMR). The study did not show a reduction in MI size with IABP, although it was postulated that this may be due to the lengthy time to revascularisation (average >180 min), which could have nullified the protective effect of LV unloading.[62]

A sub study of CRISP AMI showed a trend towards reduced mortality at 6 months with use of IABP in patients with a large MI (ST elevation > 15 mm at baseline) and persistent ischaemia (ST resolution <50% post revascularisation)[63]

PROTECT II was a randomised, prospective, multicenter study which explored the use of the of Impella CP 2.5 L in a population of patients undergoing high risk PCI. The primary end point was major adverse events (MAEs) at discharge and 30 days. 452 patients with complex 3-vessel disease or unprotected left main coronary artery disease and severely depressed left ventricular function were randomised to receive the Impella or IABP. The 2.5 L Impella undoubtedly provided superior hemodynamic support in comparison with IABP but this was not associated with any difference in outcome at 30 days (35.1% vs 40.1%, $P = 0.227$). The study was discontinued early due to futility based on observed 30-day results of the first 327 patients and only 69% of the planned 654 patients were enrolled. A post hoc analysis suggested a marginal benefit of the Impella in the 'as-treated' population – at

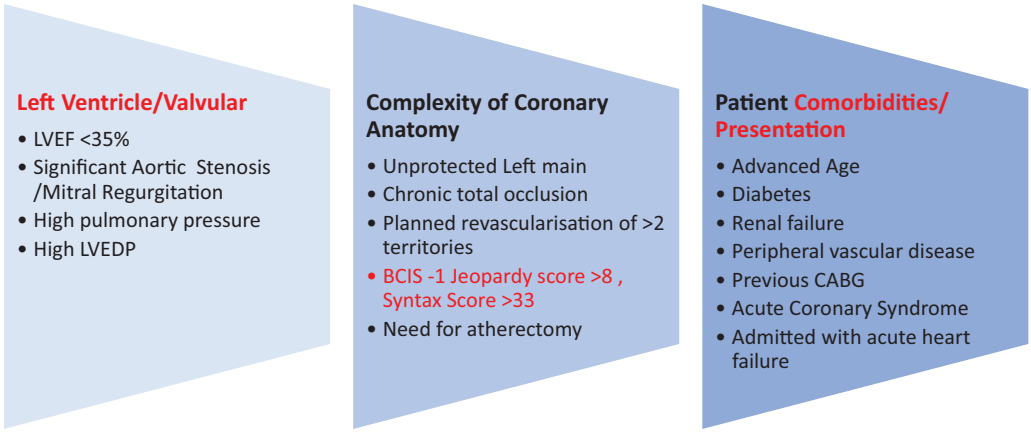

Figure 2. High risk PCI characteristics.

Table 3. Randomised clinical trials with comparison of mechanical cardiac support devices.

Trial	Patient Cohort	Device/ Devices Compared	Primary End Point	Outcomes
High risk PCI				
BCIS – 1 (2010)	High risk PCI (N = 301)	Elective IABP vs No planned IABP	MACCEs at hospital discharge or 28 days after index PCI	No significant difference in MACCEs
CRISP AMI (2011)	Anterior AMI without CS (N = 337)	IABP	If IABP insertion prior to pPCI reduced MI size (% of LV mass on CMR)	No reduction in infarct size with IABP
PROTECT II (2012)	Nonemergency High risk PCI (N = 447)	Impella vs IABP	If Impella 2.5 reduced MAEs compared to IABP at discharge or 30 day	No significant difference in MAEs at 30 day. Impella 2.5 significantly increased cardiac power compared to IABP
Cardiogenic shock				
TACTICS (2005)	CS complicating AMI (N = 57)	IABP	All cause mortality at 6 months	IABP for 48 hrs after thrombolysis did not reduce mortality. Trend towards reduced mortality with IABP in Killip Class III/IV at 6 months
Thiele et al (2005)[29]	AMI and CS (N = 41)	Tandem heart vs IABP	Improvement in CPI 2 hours after device implantation	CPI significantly incremented in Tandem Heart group. No difference in mortality at 30 day
Burkhoff et al (2006)	CS (61.9% had MI) (N = 42)	Tandem Heart vs IABP	Change in Haemodynamics (CI/MAP/PCWP)	Tandem Heart significantly augmented CI , MAP and decreased PCWP . No change in 30-day mortality.
ISAR SHOCK (2008)	CS complicating AMI (N = 25)	Impella 2.5 vs IABP	Change in CI from baseline to 30 min after device implantation	Delta change in CI was significantly greater with Impella 2.5 than IABP. 30-day mortality similar
IABP SHOCK II (2012)	Early revascularisation (PCI or CABG) in AMI complicated by CS (N = 600)	IABP	30 day all cause mortality	IABP before or immediately after revascularisation did not reduce mortality
IMPRESS (2017)	CS complicating AMI (N = 48)	Impella CP vs IABP	If Impella CP reduced 30- day mortality compared to IABP	No difference in mortality at 30 days and 6 months

CS: cardiogenic shock; AMI: acute myocardial infarction; IABP: intra aortic balloon pump; CPI: cardiac power index; CI: cardiac index; MAP: mean arterial pressure; PCWP: pulmonary capillary wedge pressure; MACCEs: major adverse cardiovascular cerebrovascular events; CMR: cardiac magnetic resonance imaging; MAEs: major adverse events; pPCI: primary percutaneous coronary intervention.

90 days, there was trend towards lower MAE's in the Impella group (40.6% vs 51.5%, P = 0.006) and a signal for more complete revascularization. Furthermore, the rate of repeat revascularisation was lower in Impella group (3.6% vs 7.8%, P = 0.056).[64]

Europella and USpella were large scale registries that evaluated safety and feasibility of Impella 2.5 in high risk PCI and measured outcomes with Impella support prior to undertaking PCI in patient with CS complicating AMI. Impella was safe to use pre PCI and allowed more complete revascularisation and improved 30 day survival.[3,59] Ameloot et al. reportedsimilar results when they retrospectively analysed 198 patients who had high risk PCI in their center – 35% had MCS implanted prior to PCI and 65% had PCI without MCS. There was improved in survival at 24 hours and 30 days in the Impella group, but clearly this study was non- randomised, and underpowered to detect meaningful differences between the two groups.[65]

However, a recent observational study by Amin et al, showed despite a significant increment in volume of Impella device usage for high risk PCI in the last decade, it remains associated with higher rates of adverse events (death, bleeding and stroke).[66]

Evidence for role VA ECMO in elective high-risk PCI is limited and stems largely from small registries and observational studies. The technology can provide sustained haemodynamic support, thereby allowing longer balloon inflation time period and more complete revascularisation at cost of higher vascular complication rates and need for more blood transfusion compared with other MCS.[67–69]

Guidelines

From available body of literature, the evidence for use of MCS in CS and high-risk PCI is weak (Table 3). Despite this, the American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) have given a Class IIb recommendation for use of MCS in elective and acute settings as an adjunct to HR PCI, depending upon the hemodynamic condition of the patient, anticipated risk of circulatory compromise during the procedure, and the need for hemodynamic support after revascularization.[33] The European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) differ from their American counterparts and recommend the short-term use of MCS only in setting of CS complicating AMI after careful consideration of patient age, co morbidities, neurological outcome and long-term prognosis (Class IIb). It does not recommend use of IABP in CS (Class III).[70]

Conclusion

There is now an array of MCS devices available which provide varying degrees of haemodynamic support during PCI. However, the theoretical benefit of haemodynamic support has not translated into improved clinical outcomes in any randomised clinical trial in patients with CS or those undergoing high risk PCI. Morbidity associated with vascular complications remains the 'Achilles heel' of all MCS devices, and the decision to use them should be based on benefit vs risk (haemodynamic gain vs vascular/bleeding complication) individualised to the patient by a 'Heart Team '. The next generation of percutaneous MCS – Impella 5.5, Aortix and intravascular ventricular assist device (iVAS) have been developed to encourage mobility and reduce vascular complication rates.[71]

In the setting of cardiogenic shock, the IABP is the only MCS device which has been studied in well-constructed trials powered for clinical endpoints. The IABP has a relatively modest effect on cardiac output and does not appear to provide sufficient haemodynamic support to affect outcome. The other MCS devices undoubtedly deliver far greater support but have been studied in only a small population of patients to date.

Of the other MCS devices, the Impella in the most widely used in CS, but less than a hundred patients have been included in randomised trials, and the data from observational studies and post commercial registries needs to be interpreted with caution. In the setting of high-risk PCI, the only randomised controlled trial (RCT) was negative and recent observational studies has shown more harm than benefit.

Numerous questions remain unanswered, not least the precise patients who may benefit from MCS use, and timing of implantation, with some feasibility studies suggesting that early (pre-PCI) use of the Impella may confer an advantage in CS. Furthermore, this population is more heterogenous than previously thought, and the new SCAI classification of CS[72] may inform the design of future studies, perhaps with a focus on those patients at the more severe end of the physiological spectrum, in whom the use of MCS may be of benefit. A similar stratification of patients undergoing high risk PCI may also provide more clarity and could help to develop a predictive risk score to guide management of patients with significant co morbidities and poor LV function who require treatment of complex coronary anatomy.

Given the current body of evidence for use of MCS is conflicting, largely from small scale randomised trials and observational studies, there has been a resurgence of interest in the field of late particularly around the Impella including proposals for new randomised trials

There are a number of ongoing studies which may help to bridge the evidence gap for MCS use, particularly in cardiogenic shock. The DanGer Shock is an adequately powered multicentre trial that will address whether MCS with Impella CP improves survival in CS.[73] EUROSHOCK is a prospective multicentre trial exploring if early ECMO intervention in patients with AMI and CS reduces mortality compared to standard treatment. The Detroit cardiogenic shock initiative was a feasibility study, has shown a significant improvement in survival to discharge results with early use of the Impella, and the National Cardiogenic Shock Initiative (NCSI) is actively recruiting to hopefully validate these results.

There is clear potential for these, and other well-constructed studies, to translate the theoretical promise of mechanical circulatory into tangible clinical benefits for these complex patient populations.

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