Use of the Impella 2.5 system alone, after and in combination with an intra-aortic balloon pump in patients with cardiogenic shock: case description and review of the literature

Roberto J. Cubeddu[1]*, MD; Rodrigo Lago[2], MD; Sofia A. Horvath[1], MD; Paul A. Vignola[1], MD; William O'Neill[3], MD; Igor F. Palacios[2], MD

1. Aventura Hospital and Medical Center, Aventura, FL, USA; 2. Massachusetts General Hospital, Boston, MA, USA; 3. University of Miami, Miami, FL, USA

KEYWORDS

- angiography
- angioplasty
- coronary flow

Abstract

Cardiogenic shock remains a serious complication of acute myocardial infarction as it is associated with very poor prognosis. Despite the historical clinical benefits of the intra-aortic balloon pump (IABP), in some patients additional mechanical cardiac support is necessary. The recent introduction of the percutaneous Impella® 2.5 mechanical circulatory support system (Abiomed Inc., Danvers, MA, USA) represents a major advancement and has been used in these circumstances. Nevertheless, the data supporting the use of this technology alone, after, or in combination with the IABP in patients with cardiogenic shock is limited and the clinical benefits remain unproven. We herein provide an updated comprehensive overview of the literature supporting the use of the Impella 2.5 system compared to the use of IABP in patients with cardiogenic shock. We also discuss the potential role for combination therapy for a patient with refractory shock. We describe a case in which an IABP was used as a bail-out strategy to provide additional haemodynamic support in a patient with refractory cardiogenic shock after the Impella 2.5 system was in place. In selected cases of refractory cardiogenic shock, the use of combined therapy with both the the Impella 2.5 and IABP can provide enhanced circulatory support and could be considered an option to maintain haemodynamic support in these patients.

* Corresponding author: Aventura Hospital & Medical Center, 20900 Biscayne Boulevard, Aventura, FL 33180, USA.
E-mail: rjcubeddu@gmail.com

Introduction

Cardiogenic shock in patients with acute coronary syndrome (ACS) carries a poor prognosis[1-4]. The optimal strategy to provide haemodynamic support in this setting involves not only prompt coronary revascularisation and use of intravenous vasopressors but also the utilisation of mechanical circulatory support therapies.

The mechanical intra-aortic balloon pump (IABP) has been historically used in these circumstances[5] to decrease left ventricular workload, augment mean arterial blood pressure, and enhance coronary blood flow[6-9]. Recently, other forms of left ventricular assist devices (LVAD) have been developed and approved including the percutaneous Impella 2.5 partial circulatory support system (Abiomed Inc., Danvers, MA, USA) for high-risk percutaneous coronary interventions (PCI) and patients with progressive haemodynamic collapse[10-16]. However, the data supporting the blanket use of this technology alone, after or in combination with the IABP in patients with cardiogenic shock is limited and remains to be proven.

We herein provide an updated comprehensive review of the literature describing the use of the novel Impella 2.5 catheter system in patients with cardiogenic shock, including comparative benefits to the IABP, and the potential value of combination therapy in a patient with refractory shock.

Percutaneous mechanical support systems: IABP and Impella 2.5

The clinical and haemodynamic value of the percutaneous Impella 2.5 and IABP system has been tested and validated in both animals and humans. However, particular emphasis has been given to the individual benefits of each technology, with only limited data comparing their actual benefits against each other or in combination in patients with cardiogenic shock. Although other percutaneous mechanical assistance devices have been introduced and tested, such as the TandemHeart® Pump (Cardiac Assist, Inc., Pittsburgh, PA, USA), and the previously used Hemopump® system (Medtronic, Inc., Minneapolis, MN, USA), their overall use has been less favourably accepted in practice because they are not user-friendly and have inherent design limitations. Thus, they are not included in the scope of this review.

IABP

The IABP was introduced in clinical practice in the early 1970s and since then multiple studies have been conducted to evaluate its haemodynamic and clinical impact in cardiogenic shock. The physiological principal includes sequential balloon counterpulsation resulting in the augmentation of diastolic and mean aortic blood pressure, and enhanced coronary perfusion[17-20]. Additional haemodynamic benefits include decrease in mean systemic impedance[21], increase in mean systemic pressure through diastolic augmentation, and reductions in left ventricular wall stress resulting in a decrease in myocardial oxygen consumption[17] **(Table 1)**.

Multiple studies have validated the clinical benefit of IABP in patients with acute coronary syndrome, cardiogenic shock, and high-risk PCI[22-27]. Based on this data, the 2004 American College of

Table 1. Mechanical and haemodynamic principles of IABP versus Impella 2.5.

	IABP	Impella 2.5
Myocardial protection		
1. ↓ Oxygen demand		
– ↓ Ventricular work by unloading[16,31-33]	–	+
– ↓ Wall tension by ↓ LVEDV and LVEDP[10,32,41]	±	+
2. ↑ Oxygen supply (↑ coronary blood flow)		
– ↑ Diastolic blood pressure[21,36,27-31]	+	+
– ↓ MV resistance by ↓ wall tension[10,29,42]	–	+
Haemodynamic support		
3. ↑ Systemic blood pressure (AoP)[19,31,32,39]	+	+
4. ↑ Cardiac output (forward flow)[16,19,21,39,43]	±	+
5. ↓ Mean systemic impedance[17,21,29]	+	+

LVEDV: left ventricular end-diastolic volume; LVEDP: left ventricular end-diastolic pressure; MV: microvascular; AoP: aortic pressure

Cardiology/American Heart Association (ACC/AHA) guidelines on ST elevation myocardial infarction (MI) recommended the use of IABP as a stabilising measure in patients with cardiogenic shock refractory to pharmacological therapy, including those with acute mitral regurgitation due to papillary muscle dysfunction/rupture, acute ventricular septal rupture, recurrent angina, poor left ventricular function, or a large area of myocardium at risk, who are being considered for prompt revascularisation. Such recommendations did not change in the 2007 focused update[28].

IMPELLA 2.5

The novel percutaneous Impella 2.5 catheter system (Abiomed Inc., Danvers, MA, USA) was introduced and cleared by the U.S. Food and Drug Administration (FDA) in 2008 under a 510(k) for use as a partial circulatory support device[11-14]. This small transvalvular catheter-mounted microaxial rotary pump actively pumps up to 2.5 litres of blood per minute from the left ventricle into the ascending aorta. Demonstrable haemodynamic results are multiple and interdependent, and include: reductions in left ventricular workload, wall tension, left ventricular end-diastolic pressure and coronary microvascular resistance, enhanced coronary perfusion, and increase in aortic antegrade blood flow, diastolic arterial pressure and mean systemic pressure[16,29-31] **(Table 1)**. These benefits were initially quantified and reported in acute animal models. Meyns et al[32] showed in an animal model that the Impella 2.5 system could reduce myocardial oxygen consumption during ischaemia, enhance reperfusion and reduce infarct size proportionally to the degree of left ventricular unloading **(Figure 1)**. Interestingly, in a calf model Reesink et al[33] demonstrated that the Impella 2.5 was superior to the IABP and resulted in more effective ventricular unloading and circulatory support. Similar comparisons have been made to evaluate the benefit of the Impella 2.5 over open chest cardiac massage in ischaemic cardiac arrest[34]. In this animal study, the percutaneous device improved myocardial perfusion, maintained cerebral
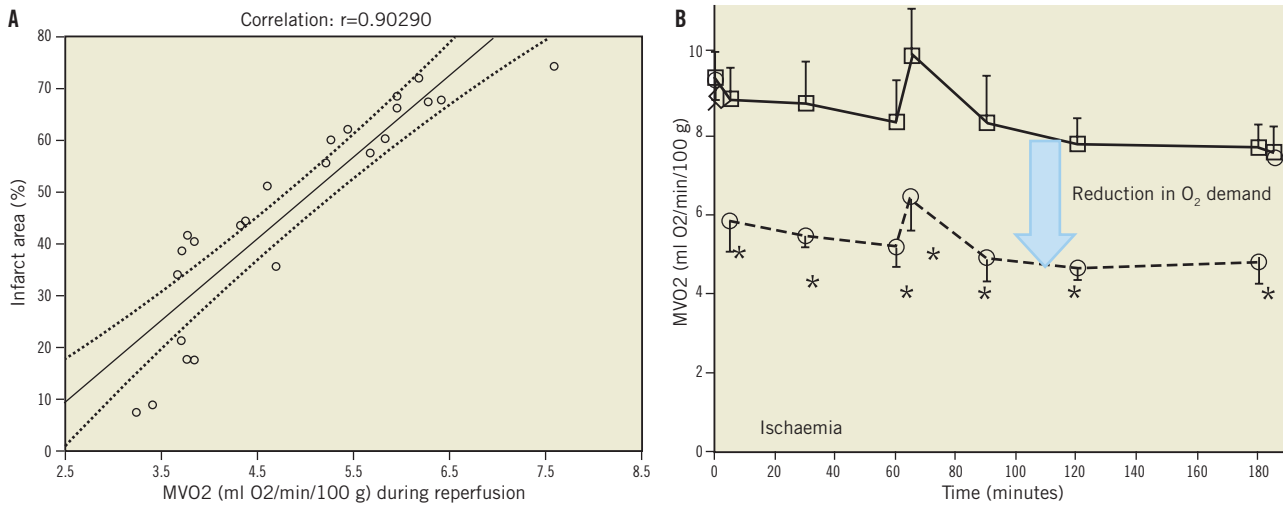
Figure 1. *Effects of left ventricular unloading during myocardial ischaemia. Panel A demonstrates strong positive correlation between infarct size and oxygen demand. Panel B shows the beneficial effects of left ventricle unloading on oxygen demand and infarct size during myocardial ischaemia. Adapted with permission from Meyns B et al[32]*

perfusion and systemic circulation with similar rates of successful defibrillation vs. cardiac massage.

Although similar benefits have been demonstrated in humans, the majority of the Impella 2.5 data involves patients undergoing high-risk PCI. In this specific group of patients, the Impella 2.5 system was proven safe and feasible, and was associated with mean increase in aortic pressure, hyperaemic coronary flow velocities, coronary perfusion, and global improvement in cardiac output[11,12,30-32,35,36]. In the results of the first U.S. multicentre registry study "USpella Registry" the Impella 2.5 was associated with significant increase in left ventricular ejection fraction (5 %), a 97 percent 30-day survival rate[37] and an improvement in New York Heart Association (NYHA) functional class in 52% of patients[41]. Moreover, lower rates of major cardiovascular events were observed when compared to standard high-risk PCI without haemodynamic support. These benefits appear to be sustained during one-year follow-up and associated with improved left ventricle (LV) ejection function[35]. The results of these and other clinical trials explain the increasing use and acceptance of this technology in a selected group of high-risk patients undergoing PCI[12,13].

Cardiogenic shock

IMPELLA 2.5

In patients with cardiogenic shock, the role of the Impella 2.5 system has been tested in only a limited number of cases and clinical trials involving non-randomised registry data **(Table 2)**. In fact, most of the data evaluating the benefits of the Impella 2.5 system in patients with cardiogenic shock derives from the experienced gathered in high-risk PCI trials. Colombo et al[15] was were some of the early authors to report the clinical benefits of the Impella 2.5 system in the setting of acute fulminant myocarditis and cardiogenic shock. During the same year, Meyns et al reported the safety,

feasibility, and efficacy of the Impella 2.5 device in 16 patients with severe cardiogenic shock, of whom 11 had failed maximal inotropic support or IABP. The authors concluded that the Impella 2.5 system results in a significant decrease in pulmonary capillary wedge pressure (29±10 mmHg to 17±5 mmHg [p=0.04]), and increase in cardiac output (4.1±1.3 l/min to 5.5±1.3 [p=0.003]), mean arterial blood pressure (57.4±13 mmHg to 74.9±13 mmHg [p=0.003]), and end-organ perfusion[16]. In a different study, Rossiter-Thornton et al highlight the role for intraoperative Impella 2.5 use during cardiopulmonary bypass withdrawal for patients with severe haemodynamic compromise, shedding some light on the value of the Impella system in other important clinical scenarios[38]. Recent expanding applications support the potential benefit of the Impella in patients undergoing high-risk balloon aortic valvuloplasty[39]. Although there are currently no randomised control trials comparing the Impella to IABP and medical therapy in patients with cardiogenic shock, the use of the Impella 2.5, according to the USpella Registry data, during post-MI cardiogenic shock, resulted in a significant increase in cardiac power output and reduced mortality[37].

IMPELLA 2.5 USE VERSUS IABP

Although several trials have supported the use of the IABP and the Impella alone in patients with cardiogenic shock, only a few studies have actually compared the benefits of one to the other. Seyfarth et al report their experience in 25 patients with cardiogenic shock following acute myocardial infarction and compare the Impella 2.5 system with IABP. In this study, the Impella 2.5 system provided superior haemodynamic support when compared to the IABP (Cardiac index after 30 min of support: 0.49 ± 0.46 l/min/m^2 vs. 0.11 ± 0.31 l/min/m^2, respectively [p=0.02]). However no significant differences were seen on 30-day mortality rates[40]. The study was however not powered for mortality.

Table 2. Studies evaluating the use of the Impella 2.5 system alone or in combination with IABP in patients with cardiogenic shock.

Author	Type of study	Sample size	Year	Results
Impella 2.5 only				
Meyns et al[16]	Case series	n=16	2003	↑ CO, ↓ mean PCWP, ↑ MAP, ↓ blood lactate.
Rossiter-Thornton et al[38]	Case report	n=1	2008	Facilitated post-operative recovery following CABG.
Impella 2.5 use versus IABP				
Reesink et al[33]	Animal study	n=8	2004	Impella offered greater ↓ in LVEDV and LVESV, and resulted in ↑ CO, mean AoP and coronary flow.
Sauren et al[42]	Animal study	n=7	2007	Impella resulted in greater ↓ in afterload, ↑ in coronary flow and ↑ AoP.
Seyfarth et al[40]	RCT	n=26	2008	Impella provided a greater ↑ CI.
Impella 2.5 use after IABP				
O'Neill et al[41]	Multicentre registry	n=352	Ongoing	Patients failing IABP had haemodynamic improvement after adding Impella with a 38% ↑ in SAP, 40% ↑ in DAP, 41% ↑ in MAP and a ↓ in PCWP and lactate level.
Impella 2.5 use combined with IABP				
Meyns et al[16]	Case series	n=16	2003	In 11/16 patients combination therapy caused: ↑ CO, ↓ mean PCWP, ↑ MAP, ↓ blood lactate.
Sauren et al[42]	Animal study	n=7	2007	Combined use resulted in enhanced coronary and carotid flow, and AoP.
Bautista-Hernández et al[35]	Case series	n=16	2007	Impella resolved cardiogenic shock in 4 of the 5 patients.
Jung et al[43]	Case report	n=1	2008	Combined use resulted in increase mean flow index, systemic BP, and ↓ blood lactate.
Gupta et al[44]	Case report	n=1	2009	The addition of Impella to IABP resulted in marked improvement in refractory CS.

AoP: aortic pressure; CABG: coronary artery bypass graft; CI: cardiac index; CO: cardiac output; CS: cardiogenic shock; RCT: randomised clinical trial; DAP: diastolic arterial pressure; IABP: intra-aortic balloon pump; LAD: left anterior descending artery; LV: left ventricle; LVEDV: left ventricular end diastolic volume; LVESV: left ventricular end systolic volume; MAP: mean arterial pressure; PCWP: pulmonary capillary wedge pressure; SAP: systolic arterial pressure

Furthermore, randomised control trials are necessary to establish superiority between both strategies in patients with cardiogenic shock. Although some may argue in favour of the haemodynamic benefits with the Impella, the scarcity of clinical data limits the determination of one strategy over the other as first line therapy in patients with cardiogenic shock.

IMPELLA 2.5 USE AFTER IABP

Despite the historic safety and efficacy data of IABP in cases of profound shock and low cardiac output, IABP often cannot independently support the systemic circulation. In such cases, haemodynamic support may be obtained using a more potent ventricular support device such as the Impella catheter pump.

In the USpella Registry[41], a total of 71 patients presented with acute myocardial infarction and cardiogenic shock. In these patients, use of the Impella increased significantly the cardiac power output and was associated with a reduction in mortality. Importantly, in a subgroup analysis of those with refractory cardiogenic shock switching from IABP to the Impella resulted in marked haemodynamic improvement, as reflected by a 38 percent increase in systolic blood pressure, 40 percent increase in diastolic blood pressure, and 41 percent increase in mean arterial pressure. Switching to the Impella improved the overall cardiac index and significantly decreased the mean wedge pressure **(Table 3)**. Thirty-day survival rates of 96 percent were observed with the use of the Impella.

Table 3. Haemodynamic effects of the Impella 2.5 system after IABP use in patients with cardiogenic shock.

Parameters	IABP	Impella after IABP
Systolic blood pressure (mmHg)	82±19	113±30
Diastolic blood pressure (mmHg)	47±16	66±16
Mean arterial pressure (mmHg)	59±15	83±17
Cardiac index (l/min/m²)	1.8	2.5
Mean ejection fraction (%)	30	34
Pulmonary wedge pressure (mmHg)	29	19

Adopted from the USpella Registry[41]

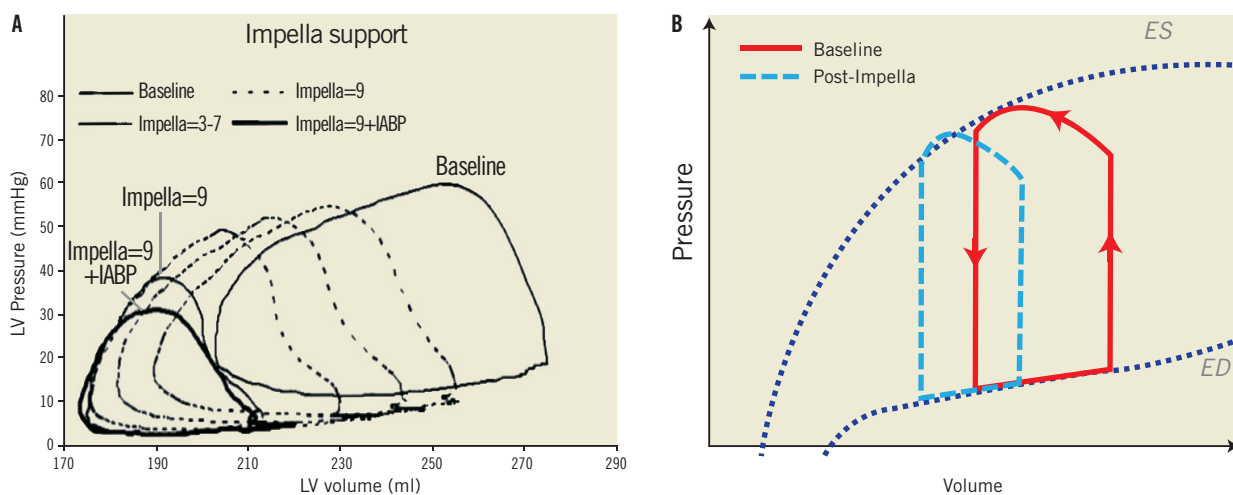## IMPELLA 2.5 USE IN COMBINATION WITH IABP

Although one could postulate that the simultaneous use of IABP and the Impella is likely superior to either strategy alone, the safety and efficacy of this approach remains clinically untested and controversial.

Interestingly, however, in a few animal studies the combined use of IABP and the Impella provided improved haemodynamic support and further enhanced myocardial perfusion when compared to either one alone. In Sauren et al's first report[42], the combined strategy resulted in enhanced systemic, cerebral, and coronary artery blood flow and further increase in mean arterial blood pressure when compared to IABP alone. Adding the Impella to the IABP caused a significant leftward shift of the pressure-volume loop
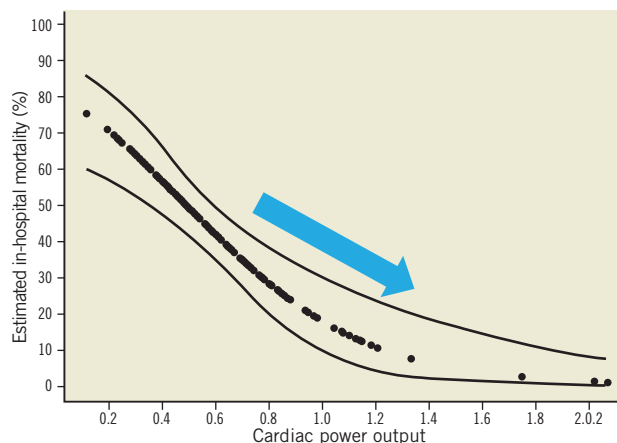
resulting in an important reduction of its area; indirectly reflecting improvement in left ventricular workload, end-diastolic pressure and myocardial oxygen demand. Each device individually contributed to the improvement seen in the myocardial oxygen "supply-demand" relationship. Importantly, the combination strategy of IABP and the Impella intensified the haemodynamic improvements beyond the benefits of either device alone **(Figure 2)**. It is thus possible that combination therapy may in fact improve overall cardiac power output, the strongest haemodynamic correlate of mortality **(Figure 3)** in cardiogenic shock[1].

Importantly, according to the expert opinion of bioengineers, forward flow of the Impella catheter system may be degraded by approximately 10 percent during diastole due to IABP-induced diastolic pressure augmentation. Nevertheless, if the goal of therapy is to increase coronary flow then combination strategy may be useful, however if the goal is to enhance forward flow, an overall reduction in the Impella flow may be seen during its simultaneous use.

The clinical experience of combination therapy is represented by a few anecdotal reports. Jung et al describe a case where combination therapy improved macrocirculation and microcirculation parameters using orthogonal polarisation spectral intravital microscope in a patient with acute myocardial infarction complicated by cardiogenic shock[43]. Subsequently, Gupta et al report a case of profound shock due to non-ischaemic cardiomyopathy. In this report, the Impella system was successfully used in combination with the IABP for haemodynamic support[44]. In both cases, the authors report significant improvement in circulatory parameters. Bautista-Hernandez et al reported a series of cases where the Impella device was used in patients with cardiogenic shock following either open heart surgery or high-risk PCI despite maximum inotropic support and use of an IABP. In this case series, the use of the Impella was safe and effective; however no benefits were seen in the subset of patients with valvular heart disease[35].

Figure 3. *Improved mortality estimates with LV Impella support. Unadjusted estimates of in-hospital mortality reduction by cardiac power output in the SHOCK trial. Adapted with permission from Fincke R et al* [1]

In this report, we describe a case of combined use of the Impella and IABP in a patient with refractory cardiogenic shock. Although limited to one case, our experience suggests that this strategy may be safe, feasible and, at times, necessary in these circumstances.

Case report

A 48-year-old man with no prior medical history presents with two-hour onset acute anterior wall myocardial infarction, resulting in acute heart failure, cardiogenic shock and severe global left ventricular systolic dysfunction with estimated ejection fraction of 10 to 15 percent. The patient was treated with full dose aspirin, intravenous heparin and BiPAP for respiratory support. Emergent cardiac catheterisation was undertaken immediately after arrival. Coronary angiography demon-

Figure 2. *Effects of Impella pump on LV wall tension and ventricular workload. Panel A shows the LV pressure and volume relationship with increasing Impella support and additional effects with IABP in ischaemic myocardium[15]. Panel B shows improvement in pressure volume loop following the effects of Impella on LV unloading. Adapted with permission from Sauren et al* [15]

strated a totally occluded proximal left main coronary artery (LMCA), with grade 2 right dominant collateral flow. Immediately following left coronary angiography, the patient developed recurrent episodes of ventricular fibrillation (VF) and asystole, requiring prolonged chest compressions, multiple shocks, temporary pacemaker placement, and airway intubation. An Impella 2.5 circulatory assist device (Abiomed Inc., Danvers, MA, USA) was promptly inserted into the left ventricle through a contralateral left femoral artery approach **(Figure 4A, Figure 4B)** providing flow rates of up to 2.2 litres per minute at a performance level of 8. Use of the Impella catheter pump resulted in immediate haemodynamic support and a sustained mean systemic arterial pressure of approximately 55 mmHg during refractory VF **(Figure 4C)**.

Percutaneous revascularisation of the LMCA was simultaneously undertaken. Throughout the procedure the patient developed repeated episodes of pulseless ventricular tachycardia (VT) and VF, during which satisfactory haemodynamic support was provided with the Impella system. Despite successful coronary revascularisation with a left main bare metal stent, continuous use of the Impella 2.5 system, and a maximum intravenous dose of neosynephrine and norepinephrine bitartrate, refractory shock persisted. An IABP was inserted through the contralateral right common femoral artery to provide enhanced circulatory support, decrease left ventricular workload and improve diastolic systemic perfusion pressure, as shown in

Figure 4D, Figure 4E and **Figure 4F**. The simultaneous use of the IABP and Impella catheter was maintained safely for 72 hours and resulted in no apparent complications or device malfunction. Haemodynamic stability was clinically acknowledged during combination therapy and represented by the decreasing dose requirements of intravenous pressors. Echocardiographic examination 48 hours from date of intervention revealed correct Impella catheter placement yet no improvement in left ventricular systolic function. Unfortunately, despite enormous efforts and continued improvement of haemodynamic measurements, the patient's hospital course was complicated by persistent multi-organ failure and sepsis resulting in death four days later.

Conclusions

Although a substantial and increasing number of data exists to support the use of IABP or the Impella system in patients with cardiogenic shock, additional clinical studies will be necessary to further understand the efficacy and safety of these strategies when used in combination. This review summarises the available experience that has been gained to date with the novel Impella mechanical LV support pump in patients with cardiogenic shock, providing insight to its potential clinical role when compared to or combined with conventional IABP. This case report is one of the very few to describe the safety and feasibility of the combined use of the Impella 2.5 and
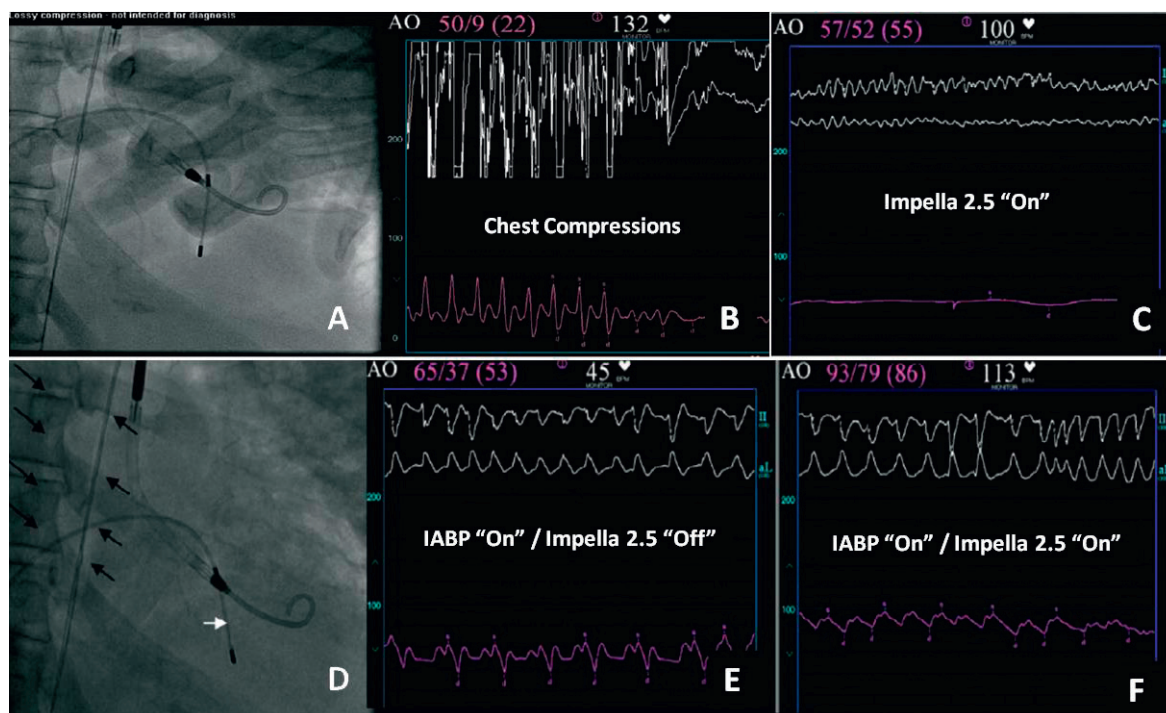
Figure 4. *Panel A: Impella 2.5 catheter across the aortic valve into the left ventricle during cardiac arrest and chest compressions. Panel B: Pressure waveform obtained during manual compression (Impella in "Off" position); mean arterial pressure 22 mmHg. Panel C: Pressure wave form obtained with the Impella 2.5 during ventricular fibrillation; notice the linear continuous waveform with mean pressure of 55 mmHg. Panel D: Insertion of IABP (black arrows) in addition to Impella to improve haemodynamic support and coronary perfusion following successful revascularisation; temporary pacer wire (white arrow). Panel E: Haemodynamic support obtained with IABP only (Impella catheter in "Off" position); mean aortic pressure 53 mmHg. Panel F: Haemodynamic support during simultaneous use of IABP and Impella 2.5; notice improvement in mean aortic pressure of 86 mmHg.*

IABP in refractory cardiogenic shock. Although it is intuitive to believe that the simultaneous use of both the Impella and IABP results in enhanced haemodynamic support during refractory shock, it is also possible that their combined use may in fact be counterproductive. Ultimately, further studies will be necessary to evaluate the potential applicability of this and other approaches.

Acknowledgements

Conflict of interest statement

References

1. Fincke R, Hochman JS, Lowe AM, Menon V, Slater JN, Webb JG, LeJemtel TH, Cotter G, for the SHOCK Investigators. Cardiac power is the strongest hemodynamic correlate of mortality. *J Am Coll Cardiol.* 2004;44:340-348.

2. Goldberg RJ, Gore JM, Alpert JS, Osganian V, de Groot J, Bade J, Chen Z, Frid D, Dalen JE. Cardiogenic shock after acute myocardial infarction–incidence and mortality from a community wide perspective 1975-1988. *N Engl J Med.* 1991;325:1117-22.

3. Holmes DR Jr, Bates ER, Kleiman NS, Sadowski Z, Horgan JH, Morris DC, Califf RM, Berger PB, Topol EJ. Contemporary reperfusion therapy for cardiogenic shock: the GUSTO-I trial experience. *J Am Coll Cardiol.* 1995;26:668-74.

4. Goldberg RJ, Samad, NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM. Temporal trends in cardiogenic shock complicating acute myocardial infarction. *N Engl J Med.* 1999;340:1162-1168.

5. Kantrowitz A, Tjonneland S, Freed PS, Phillips SJ, Butner AN, Sherman JL Jr. Initial clinical experience with intraaortic balloon pumping in cardiogenic shock. *JAMA.* 1968;203: 113-18.

6. Dormandy JA, Goetz RH, Kripke DC. Hemodynamics and coronary blood flow with counterpulsation. *Surgery.* 1969;65: 311-20.

7. Moulopoulos SD, Topaz S, Kolff WJ. Diastolic balloon pumping (with carbon dioxide) in the aorta - a mechanical assistance to the failing circulation. *Am Heart J.* 1962;63:669-75.

8. Kahn JK, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Hartzler GO. Supported high-risk coronary angioplasty using intraaortic balloon pump counterpulsation. *J Am Coll Cardiol.* 1990;15:1151-5.

9. Bregman D, Casarella WJ. Percutaneous intraaortic balloon pumping: Initial clinical experiences. *Ann Thorac Surg.* 1980;29:153-5.

10. Remmelink M, Sjauw KD, Henriques JP, de Winter RJ, Vis MM, Koch KT, Paulus WJ, de Mol BA, Tijssen JG, Piek JJ, Baan J Jr. Effects of mechanical left ventricular unloading by Impella on left ventricular dynamics in high-risk and primary percutaneous coronary intervention patients. *Catheter Cardiovasc Interv.* 2010;75:187-94.

11. Henriques JP, Remmelink M, Baan J Jr, van der Schaaf RJ, Vis MM, Koch KT, Scholten EW, de Mol AJ, Tijssen JG, Piek JJ, de Winter RJ. Safety and feasibility of elective high-risk percutaneous coronary intervention procedures with left ventricular support of the Impella Recover LP 2.5. *Am J Cardiol.* 2006;97:990-2.

12. Sjauw KD, Konorza T, Erbel R, Danna PL, Viecca M, Minden H, Butter C, Engstrøm T, Hassager C, Machado FP, Pedrazzini G, Wagner DR, Schamberger R, Kerber S, Mathey DG, Schofer J, Engström AE, Henriques JP. Supported high-risk percutaneous coronary intervention with the Impella 2.5 device the Europella registry. *J Am Coll Cardiol.* 2009;54:2430-4.

13. Dixon SR, Henriques JP, Mauri L, Sjauw K, Civitello A, Kar B, Loyalka P, Resnic FS, Teirstein P, Makkar R, Palacios IF, Collins M, Moses J, Benali K, O'Neill W. A Prospective Feasibility Trial Investigating the Use of the Impella 2.5 System in Patients Undergoing High-Risk Percutaneous Coronary Intervention (The PROTECT I Trial): Initial U.S. Experience. *J Am Coll Cardiol Intv.* 2009;2:91-96.

14. Sjauw KD, Remmelink M, Baan J Jr, Lam K, Engström AE, van der Schaaf RJ, Vis MM, Koch KT, van Straalen JP, Tijssen JG, de Mol BA, de Winter RJ, Piek JJ, Henriques JP. Left ventricular unloading in acute STEMI patients is safe and feasible and provides acute and sustained left ventricular recovery. The AMC MACH 2 study. *J Am Coll Cardiol.* 2008; 51:1044-1046.

15. Colombo T, Garatti A, Bruschi G, Lanfranconi M, Russo C, Milazzo F, Catena E, Frigerio M, Vitali E. First successful bridge to recovery with the impella Recover 100 left ventricular assist device for fulminant acute myocarditis. *Ital Heart J.* 2003;4:642-645.

16. Meyns B, Dens J, Sergeant P, Herijgers P, Daenen W, Flameng W. Initial experiences with the Impella device in patients with cardiogenic shock - Impella support for cardiogenic shock. *Thorac Cardiovasc Surg.* 2003;51:312-317.

17. Mueller H, Ayres SM, Conklin EF, Giannelli S Jr, Mazzara JT, Grace WT, Nealon TF Jr. The effects of intra-aortic counterpulsation on cardiac performance and metabolism in shock associated with acute myocardial infarction. *J Clin Invest.* 1971;50:1885.

18. Kern MJ, Aguirre FV, Tatineni S, Penick D, Serota H, Donohue T, Walter K. Enhanced coronary blood flow velocity during intraaortic balloon counterpulsation in critically ill patients. *J Am Coll Cardiol.* 1993;21:359-68.

19. Scheidt S, Wilner G, Mueller H, Summers D, Lesch M, Wolff G, Krakauer J, Rubenfire M, Fleming P, Noon G, Oldham N, Killip T, Kantrowitz A. Intra-Aortic Balloon Counterpulsation in Cardiogenic Shock – Report of a Cooperative Clinical Trial. *N Engl J Med.* 1973;288:979-84.

20. Kern MJ, Aguirre F, Bach R, Donohue T, Siegel R, Segal J. Augmentation of coronary blood flow by intra-aortic balloon pumping in patients after coronary angioplasty. *Circulation.* 1993;87:500-11.

21. Urschel CW, Eber L, Forrester J, Matloff J, Carpenter R, Sonnenblick E. Alteration of mechanical performance of the ventricle by intraaortic balloon counterpulsation. *Am J Cardiol.* 1970;25:546-51.

22. Ishihara M, Sato H, Tateishi H, Uchida T, Dote K. Intraaortic balloon pumping as the postangioplasty strategy in acute myocardial infarction. *Am Heart J.* 1991;122:385-9.

23. Flaherty JT, Becker LC, Weiss JL, Brinker JA, Bulkley BH, Gerstenblith G, Kallman CH, Weisfeldt ML. Results of a rand-

omized prospective trial of intraaortic balloon counterpulsation and intravenous nitroglycerin in patients with acute myocardial infarction. *J Am Coll Cardiol*. 1985;6:434-46.

24. Stone GW, Marsalese D, Brodie BR, Griffin JJ, Donohue B, Costantini C, Balestrini C, Wharton T, Esente P, Spain M, Moses J, Nobuyoshi M, Ayres M, Jones D, Mason D, Grines L, O'Neill WW, Grines CL. A prospective, randomized evaluation of prophylactic intraaortic balloon counterpulsation in high risk patients with acute myocardial infarction treated with primary angioplasty. Second Primary Angioplasty in Myocardial Infarction (PAMI-II) Trial Investigators. *J Am Coll Cardiol*. 1997;29:1459-67.

25. Brodie BR, Stuckey TD, Hansen C, Muncy D. Intra-aortic balloon counterpulsation before primary percutaneous transluminal coronary angioplasty reduces catheterization laboratory events in high-risk patients with acute myocardial infarction. *Am J Cardiol*. 1999;84:18-23.

26. Mishra S, Chu WW, Torguson R, Wolfram R, Deible R, Suddath WO, Pichard AD, Satler LF, Kent KM, Waksman R. Role of prophylactic intra-aortic balloon pump in high-risk patients undergoing percutaneous coronary intervention. *Am J Cardiol*. 2006;98:608-12.

27. Lincoff AM, Popma JJ, Ellis SG, Vogel RA, Topol EJ. Percutaneous support devices for high risk or complicated coronary angioplasty. *J Am Coll Cardiol*. 1991;17:770-80.

28. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, Hochman JS, Krumholz HM, Lamas GA, Mullany CJ, Pearle DL, Sloan MA, Smith SC Jr; 2004 Writing Committee Members, Anbe DT, Kushner FG, Ornato JP, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Halperin JL, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B, Tarkington LG, Yancy CW. 2007 focused update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction). *Circulation*. 2008;117:296-329

29. Remmelink M, Sjauw KD, Henriques JP, de Winter RJ, Koch KT, van der Schaaf RJ, Vis MM, Tijssen JG, Piek JJ, Baan J Jr. Effects of left ventricular unloading by Impella Recover LP2.5 on coronary hemodynamics. *Cathet Cardiovasc Interv*. 2007;70:532-537.

30. Aqel RA, Hage FG, Iskandrian AE. Improvement of myocardial perfusion with a percutaneously inserted left ventricular assist device. *J Nucl Cardiol*. 2010;17:158-60.

31. Valgimigli M, Steendijk P, Sianos G, Onderwater E, Serruys PW. Left ventricular unloading and concomitant total cardiac output increase by the use of percutaneous Impella Recover LP 2.5 assist device during high-risk coronary intervention. *Cathet Cardiovasc Interv*. 2005;65:263-267.

32. Meyns B, Stolinski J, Leunens V, Verbeken E, Flameng W. Left ventricular support by catheter-mounted axial flow pump reduces infarct size. *J Am Coll Cardiol*. 2003;41:1087-1095.

33. Reesink KD, Dekker AL, Van Ommen V, Soemers C, Geskes GG, van der Veen FH, Maessen JG. Miniature intracardiac assist device provides more effective cardiac unloading and circulatory support during severe left heart failure than intraaortic balloon pumping. *Chest*. 2004;126:896-902.

34. Tuseth V, Pettersen RJ, Grong K, Wentzel-Larsen T, Haaverstad R, Fanneløp T, Nordrehaug JE. Randomised comparison of percutaneous left ventricular assist device with open-chest cardiac massage and with surgical assist device during ischaemic cardiac arrest. *Resuscitation*. 2010;81:1566-70.

35. Bautista-Hernández V, Gutiérrez F, Pinar E, Gimeno JR, Arribas JM, García-Puente J, Ray VG, Arcas R, Valdés M. Initial experience with the Impella left ventricular assist device for post-cardiotomy cardiogenic shock and unprotected left coronary artery angioplasty in patients with a low left ventricular ejection fraction. *Rev Esp Cardiol*. 2007;60:984-987.

36. Burzotta F, Paloscia L, Trani C, Mascellanti M, Mongiardo R, Materazzo G, Niccoli G, Di Marco M, Leone AM, Porto I, Mazzari MA, Rebuzzi AG, Schiavoni G, Crea F. Feasibility and long-term safety of elective Impella-assisted high-risk percutaneous coronary intervention: a pilot two-centre study. *J Cardiovasc Med*. 2008;9:1004-1010.

37. Abiomed, Inc. (2009). Abiomed Presents Results From Two Studies: USpella and MACH II [Press release]. Retrieved from http://www.cathlabdigest.com/Abiomed-Presents-Results-From-Two-Studies-USpella-and-MACH-II.

38. Rossiter-Thornton M, Arun V, Forrest AP, Bayfield MS, Wilson MK. Left Ventricular Support with the Impella® LP 5.0 for Cardiogenic Shock Following Cardiac Surgery. *Heart Lung Circ*. 2008;17:243-5.

39. Londoño JC, Martinez CA, Singh V, O'Neill WW. Hemodynamic support with Impella 2.5 during balloon aortic valvuloplasty in a high-risk patient. *J Interv Cardiol*. 2011;24:193-7.

40. Seyfarth M, Sibbing D, Bauer I, Fröhlich G, Bott-Flügel L, Byrne R, Dirschinger J, Kastrati A, Schömig A. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. *J Am Coll Cardiol*. 2008;52:1584-1588.

41. O'Neill WW from Abiomed, Inc. (2010). Abiomed's USpella Results Presented at EuroPCR [Press release]. Retrieved from http://bmctoday.net/citoday/2010/04/article.asp?f=abiomeds-uspella-results-presented-at-europcr.

42. Sauren LD, Accord RE, Hamzeh K, de Jong M, van der Nagel T, van der Veen FH, Maessen JG. Combined Impella and intraaortic balloon pump support to improve both ventricular unloading and coronary blood flow for myocardial recovery: an experimental study. *Artif Organs*. 2007;31:839-42.

43. Jung C, Ferrari M, Rödiger C, Fritzenwanger M, Figulla HR. Combined Impella and intra-aortic balloon pump support to improve macro- and microcirculation: a clinical case. *Clin Res Cardiol*. 2008;97:849-50.

44. Gupta A, Allaqaband S, Bajwa T. Combined use of impella device and intra-aortic balloon pump to improve survival in a patient in profound cardiogenic shock post cardiac arrest. *Catheter Cardiovasc Interv*. 2009;74:975-6.