

Initial experience covering 50 consecutive cases of large Impella implantation at a single heart centre

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Abstract

Aims Pre-operative or post-operative heart failure (HF) and cardiogenic shock of various natures frequently remain refractory to conservative treatment and require mechanical circulatory support. We report our clinical experience with large Impella systems (5.0 or 5.5; i.e. Impella 5+) (Abiomed Inc., Boston, USA) and evaluate the parameters that determined patient outcome.

Methods and results The initial 50 cases of Impella 5+ implanted for acute HF between November 2018 and August 2020 at a single centre were enrolled in this study. Data, including preoperative characteristics, perioperative clinical course information, and post-operative outcomes, were retrospectively collected from the hospital data management and quality assurance system. Descriptive and univariate analyses were performed. Among the 49 patients in this study, 28 (56.0%) survived in the first 30 days post-operatively, and 3 died of non-cardiac reasons later. In-hospital mortality was significantly higher in patients with biventricular failure [$P < 0.01$, odds ratio (OR) 5.63] or dilated cardiomyopathy (DCM) ($P = 0.02$, OR 15.8), whereas ischaemic cardiomyopathy (ICM) was associated with lower mortality ($P = 0.03$, OR 0.24). Interestingly, the mortality was comparable between the 'solo' Impella group and the veno-arterial extracorporeal membrane oxygenation (va-ECMO) plus Impella (ECMELLA) group, despite the severity of the patients' profile in the ECMELLA group ('solo' vs. ECMELLA; 55.6% vs. 52.6%, $P = 1.00$). All patients who received an additional temporary right ventricular assist device (tRVAD) were successfully weaned from va-ECMO.

Conclusions Our results suggest that biventricular failure and DCM are predictors of higher mortality in patients with Impella. Considering the pathophysiology of HF, implantation of a large Impella system seems to be promising, especially for ICM patients. The large Impella system might be more effective for better prognosis of patients under va-ECMO, and combination therapy with tRVAD seems to be a promising strategy for early weaning from va-ECMO.

Keywords Cardiogenic shock; Impella; Extracorporeal membrane oxygenation; Coronary artery bypass

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Introduction

Pre-operative or post-operative heart failure (HF) and cardiogenic shock (CS) due to various types of myocarditis occasionally remain refractory to conservative treatment. In such clinical situations, percutaneous insertion of cardiovascular

devices has gained significant interest. Because the clinical outcome of intra-aortic balloon pumping in randomized controlled trials has been disappointing,^{1–3} veno-arterial extracorporeal membrane oxygenation therapy (va-ECMO) has become the preferred option for mechanical circulatory support (MCS) for sustained CS. However, va-ECMO support

increases cardiac afterload, which may lead to enhanced left ventricular (LV) congestion, pulmonary oedema, and secondary right HF.

The different Impella systems available today (Abiomed Inc., Boston, USA) provide antegrade flow and additional LV unloading to reduce myocardial oxygen demand and increase coronary perfusion. These considerations imply that Impella therapy may provide a less invasive and superior option for LV recovery. Impella therapy allows early patient extubation and mobilization. In this sense, Impella would be valued not only for 'bridge to recovery' but also for 'bridge to therapy' or 'bridge to candidacy', so that the clinical condition of CS patients can be prepared for a more durable therapy; a concept that has been referred to as 'preconditioning'. Particularly in the field of cardiac surgery, attention has been focused on large Impella systems, that is, Impella 5.0 or Impella EU/5.5 (Impella 5+), which can provide full support and function as a temporary left ventricular assist device (LVAD). Therefore, Impella 5+ is expected to act as a proper physiological MCS device in the context of the complex pathophysiology of CS. At our institute, Impella 5+ has been utilized since November 2018. As reports on the clinical results of Impella 5+ are limited, we would like to share our initial experience with the first 50 consecutive cases treated with Impella 5+. Herein, we evaluated the clinical outcome and analysed the risk factors that may influence mortality in order to elucidate the usefulness of the large Impella system as a temporary MCS.

Materials and methods

Ethics committee approval

This study was approved by the Ethics Committee of the Medical Faculty of the Heinrich Heine University Düsseldorf (Ref.2020-1173).

Study population, word definitions, and data collection

Fifty-nine Impella 5+ ($n = 57$ for Impella 5.0; $n = 2$ for Impella 5.5) were implanted during 50 independent treatments due to HF in 49 consecutive patients between November 2018 and August 2020 at a single institution. Clinical, procedural, and laboratory data were collected for this retrospective observational study. Reimplantation of Impella 5+ was performed because of pump dysfunction in six patients (thrombosis or dislocation in four and two patients, respectively, including 'downgrade' from Impella 5.5 to 5.0 in $n = 1$). Moreover, Impella was upgraded from 5.0% to 5.5% in one patient after 7 weeks of Impella 5.0. Furthermore, three patients had a second Impella 5.0 implantation in the observation period

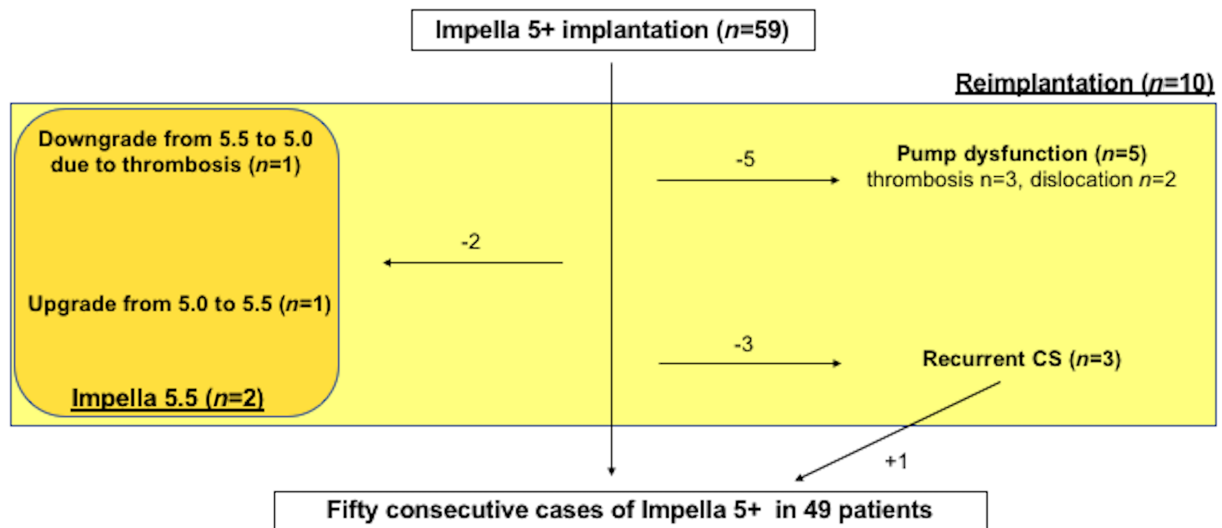
for different reasons, including one readmission due to CS after successful discharge after the first treatment. The latter patient received Impella 5.0 after acute decompensation due to periprocedural complications during implantation of an internal cardioverter-defibrillator 7 months after their first successful Impella 5.0 treatment and discharge from our department. Two independent Impella treatments in this particular patient were counted as two cases for the purpose of this study. Thus, we evaluated clinical outcomes and analysed the risk factors that influenced mortality in 50 consecutive Impella 5+ cases (Figure 1).

For the classification of patients with CS, the interagency registry for mechanically assisted circulatory support (INTERMACS) profile was used as an indicator of the general condition of preoperative patients. In addition, we categorized the following three therapy concepts to allocate all cases according to the indication of Impella implantation in this study (intention-to-treat):

- 1 Group 1, the 'bridge to candidacy/transplant/decision' group, referred to patients with impaired cardiocirculatory stability under conservative therapy, including inotropic support necessitating therapy escalation, who were not candidates for the implantation of a permanent ventricular assist device. These patients may have become eligible for LVAD implantation after the resolution of contraindications ('bridge to candidacy') or may have carried absolute and permanent contraindications for LVAD but were well eligible for orthotopic heart transplantation (oHTX) once an appropriate organ became available ('bridge to transplant'). Finally, in some patients, circulatory support was needed to complete the patient profile assessment in order to make a solid decision regarding more durable therapy solutions ('bridge to decision').
- 2 Group 2, the 'bridge to recovery' group, referred to patients for whom a clear perception of the actual disease pattern (including underlying causal elements) existed and who, according to the assessment of the managing team, were likely to experience short-term improvement of cardiac function with or without invasive or conservative treatment. Most of the patients in this group underwent open-heart operations or interventional therapy, but they needed Impella support to stabilise circulation in the periprocedural period.
- 3 Group 3, the 'planned perioperative support', included patients who presented with severely impaired LV function in an urgent but planned setting prior to cardiac surgery. Impella was implanted in a planned perioperative setting to promote post-operative recovery.

In-hospital mortality was defined as death during the first hospitalisation, whereas 30 day survival was defined as survival at 30 days after Impella 5+ implantation. Right ventricular failure (RVF) was defined as having at least

Figure 1 The graphic explanation of study population. Fifty cases in 49 patients, arising from 59 Impella 5+ (5.0 or 5.5) implantation. CS, cardiogenic shock.



moderate RV impairment on the echocardiographic evaluation according to the guidelines of the European Society of Cardiology. All data, including preoperative characteristics, perioperative clinical course information, and post-operative outcomes, were retrospectively collected from the hospital data management and quality assurance system.

Surgical procedure

All patients underwent a surgical approach with the insertion of Impella 5+ via a 10 mm prosthesis chimney implanted in an end-to-side fashion to the right subclavian artery ($n = 51$, 86.0%) or femoral artery ($n = 8$, 14.0%). Insertion and final positioning were monitored using fluoroscopy and transoesophageal echocardiography.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences® (SPSS) 25.0 (IBM, Chicago, USA). Using this programme, descriptive and comparative (χ^2 test, Mann–Whitney U -test) statistics were performed. However, Fisher's exact test was adapted instead of the χ^2 test for a minimum expected value of less than five. The data of interval-scaled variables are expressed as mean \pm standard deviation. Statistical significance was set at $P < 0.05$. For the intensity of the correlation coefficient, phi was indicated. A value greater than $|0.25|$ was considered as a strong correlation.

Results

Baseline clinical characteristics

The baseline clinical characteristics of the 50 patients are shown in *Table 1*. Eighty-four per cent were male patients in 42 cases and 16.0% female patients in 8 cases, with a mean age of 61.1 ± 11.7 years at the time of Impella implantation. The most common underlying disease for Impella implantation was ischaemic cardiomyopathy (ICM) ($n = 35$, 70.0%), followed by dilated cardiomyopathy (DCM; $n = 8$, 16.0%). Concerning disease severity according to the INTERMACS profiles,⁴ 60% of all cases were allocated to the lowest profile groups (INTERMACS 1, 32%; INTERMACS 2, 28%). In 38 cases, a combination of va-ECMO plus Impella, referred to as 'ECMELLA', was employed, with va-ECMO implanted prior to Impella implantation in almost all ECMELLA cases in this report ($n = 36$ out of 38, i.e., 94.7%). An additional temporary right ventricular assist device (tRVAD) was needed in 9 patients, 6 of whom had a TandemHeart ProtekDuo (LivaNova, CardiacAssist Inc., Pittsburgh, USA) inserted for post-operative management.

In all 10 cases of Impella 5, reimplantation was performed through the same access that was used in the Impella implantation index, with no complications associated with re-exploration of the artery or Impella exchange. During the exchange operation, the pre-existing vascular graft was largely resected, leaving a about 10–15 mm broad proximal ring, which was then anastomosed to a fresh vascular graft. In only one case, the entire vascular graft used for the previous Impella insertion was removed before anastomosis of the

new graft. Flashing of the native artery and the Fogarty manoeuvre for removal of the wall-adhering thrombus formation was applied in all cases.

Table 1 Baseline clinical characteristics

	Cases (n = 50)
Age (years)	61.1 ± 11.7
Male, n (%)	42 (84.0)
Arterial hypertension, n (%)	29 (58.0)
Hyperlipidaemia, n (%)	13 (26.0)
Diabetes, n (%)	17 (34.0)
Peripheral vascular disease, n (%)	4 (8.0)
Arrhythmia, n (%)	17 (34.0)
COPD, n (%)	3 (6.0)
Nicotine abuses, n (%)	13 (26.0)
Drug abuses, n (%)	2 (4.0)
Dialysis, n (%)	2 (4.0)
History of PCI, n (%)	16 (32.0)
Post-CPR, n (%)	12 (24.0)
Biventricular failure, n (%)	28 (56.0)
ICM, n (%)	35 (70.0)
DCM, n (%)	8 (17.0)
Myocarditis, n (%)	2 (4.0)
CS after oHTX, n (%)	2 (4.0)
INTERMACS profiles, n (%)	
I: critical cardiogenic shock	16 (32.0)
II: progressive decline	14 (28.0)
III: stable but inotrope dependent	17 (34.0)
IV: resting symptoms	1 (2.0)
V: exertion intolerant	2 (4.0)
Therapy concept, n (%)	
1. bridge to candidacy/transplant/decision	21 (42.0)
2. bridge to recovery	26 (52.0)
3. planned perioperative support	3 (6.0)
va-ECMO implantation, n (%)	38 (76.0)
Prior to Impella	36 (72.0)
Upgrade from Impella CP, n (%)	8 (17.0)

COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; CS, cardiogenic shock; DCM, dilatative cardiomyopathy; ICM, ischaemic cardiomyopathy; INTERMACS, interagency registry for mechanically assisted circulatory support; oHTX, orthotopic heart transplantation; PCI, percutaneous coronary intervention; va-ECMO, venous-arterial extracorporeal membrane oxygenation.

Data documented as n (%) or mean ± standard deviation.

Clinical outcome of Impella 5+

The overall clinical outcomes are shown in *Table 2*. A total of 28 cases (56.0%) survived the first 30 days after Impella implantation, but 3 died of non-cardiac reasons later (after 45, 73, and 210 days, respectively). Of the remaining 25 cases, 14 cases recovered without any other escalation therapy, and Impella was explanted on post-operative day 11.1 ± 5.19. Among the remaining 11 cases, 3 required additional tRVAD (TandemHeart) for eventual recovery after 15.7 ± 6.34 days, whereas the remaining 8 patients underwent either permanent LVAD implantation (n = 6, four of them with tRVAD) or were directly bridged to oHTX (n = 2, one of them with tRVAD). In addition, oHTX was also applied in two cases who underwent permanent LVAD implantation (n = 2/6, 33.3% of LVAD recipients) after 31 and 444 days of LVAD support (*Figure 2*). In the entire cohort, therapy withdrawal was performed due to cerebral vascular accidents in six cases representing 24.0% of all in-hospital mortality (n = 25). All the latter cases died within 24 h after Impella withdrawal.

We analysed in-hospital mortality in subgroups stratified according to the INTERMACS profile as well as the therapy concept at the time of Impella implantation (*Table 3*). Interestingly, the in-hospital mortality rates of INTERMACS Groups 1 and 2 were almost the same. In contrast, in the ‘planned perioperative support’ group, including patients in the INTERMACS Groups 4 and 5, there was no in-hospital mortality. Of note, in this group, all three patients underwent Impella 5.0 implantation to provide intraoperative circulatory stability during planned beating heart coronary artery bypass grafting (CABG) in the presence of severe LV dysfunction. All three patients fully recovered after 8.7 ± 4.0 days of Impella support and were discharged home on post-operative day 27.0 ± 3.46 without any complications. The total operation time was 388.3 ± 39.5 min, with an average of three grafts performed

Table 2 Clinical outcome on Impella support

	Cases		
	All (n = 50)	D (n = 25)	S (n = 25)
30 day survival, n (%)	28 (56.0)		
In-hospital mortality, n (%)	25 (50.0)		
	Due to MOF, n (%)	19 (76.0)	
	Due to CVA, n (%)	6 (24.0)	
Successful weaning without escalation therapy, n (%)			14 (56.0)
Successful escalation therapy, n (%)			11 (44.0)
	Percutaneous RVAD, n (%)		3 (12.0)
	Permanent LVAD, n (%)		6 (24.0)
	oHTX, n (%)	Direct/post LVAD	2 (8.0)/2(8.0)

CVA, cerebral vascular accident; D, dead group; INTERMACS, interagency registry for mechanically assisted circulatory support; LVAD, left ventricular assist device; MOF, multiple organ failure; oHTX, orthotopic heart transplantation; RVAD, right ventricular assist device; S, survival group.

Data documented as n (%).

Figure 2 The diagram of clinical outcome in all cases. LV, left ventricle; LVAD, left ventricular assist devices; MCS, mechanical circulatory support; oHTX, orthotopic heart transplantation; tRVAD, temporary right ventricular assist device; w/, with.

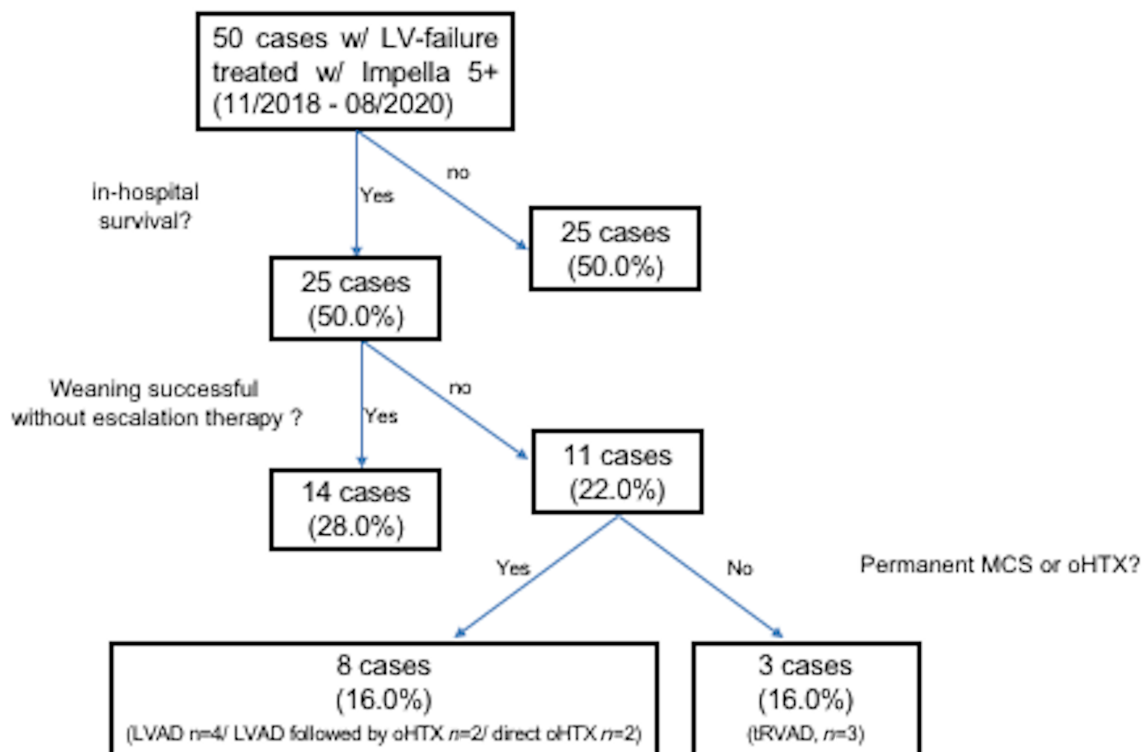


Table 3 In-hospital mortality of subgroups based on INTERMACS profile and therapy concept

Therapy concept	INTERMACS profile										Total, n		Mortality (%)
	I		II		III		IV		V				
	S	D	S	D	S	D	S	D	S	D	S	D	
1. Bridge to candidacy/transplant/decision, n (%)	3	3 (50.0)	4	4 (50.0)	4	3 (42.9)					11	10	47.6
2. Bridge to recovery, n (%)	4	6 (60.0)	2	4 (66.7)	5	5 (50.0)					11	15	57.7
3. Planned perioperative support, n (%)							1	0 (0)	2	0 (0)	3	0	0.0
Total, n	7		6	8	9	8	1	0	2	0	25	25	50.0
Mortality (%)		56.3		57.1		47.1		0.0		0.0			50.0

D, dead group; INTERMACS, interagency registry for mechanically assisted circulatory support; S, survival group. Data documented as n (%).

during surgical revascularization. The left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD) improved (LVEF; $21.7 \pm 2.89\%$ vs. $29.7 \pm 0.58\%$, LVEDD; 62.0 ± 8.00 mm vs. 58.3 ± 3.51 mm, pre vs. post, respectively).

Univariable analysis of predictive factors for mortality in patients receiving Impella 5+

We classified all cases into survival vs. death groups. Concerning INTERMACS profiles, we divided all cases into

two groups of lower profile (Profiles 1 and 2, $n = 30$) vs. higher-profile group (Profile 3 and other, $n = 20$). We then conducted a univariate analysis of predictive factors for mortality in all cases (Table 4).

Statistically significant differences in predictive factors for mortality were evident in patients with biventricular failure or DCM ($P < 0.01$, and $P = 0.02$, respectively) with a very strong correlation coefficient ($\phi = 0.40$ and $\phi = 0.55$, respectively). In contrast, ICM had a statistically significant benign prognosis in the setting of Impella 5+, with a strong correlation ($P = 0.03$, $\phi = -0.31$). In the latter cohort, 28 patients underwent revascularization with PCI ($n = 7$) or CABG

Table 4 Univariable analysis of predictive factors for in-hospital mortality on Impella 5+

	Survival (n = 25)		Dead (n = 25)		χ^2	df	P	phi
Age (years)	57.6 ± 14.7		61.5 ± 7.42				0.59	
Male, n (%)	4	16.0	4	16.0	0.00	1	1.00	
Arterial hypertension, n (%)	10	40.0	11	44.0	0.08	1	0.77	
Hyperlipidaemia, n (%)	8	32.0	5	20.0	0.94	1	0.33	
Diabetes, n (%)	9	36.0	8	32.0	0.09	1	0.77	
Peripheral vascular disease, n (%)	3	12.0	1	4.0	1.09	1	0.61	
Arrhythmia, n (%)	6	24.0	11	44.0	2.23	1	0.14	
COPD, n (%)	2	8.0	1	4.0	0.36	1	1.00	
Drug abuses, n (%)	2	8.0	0	0.0	2.08	1	0.49	
Dialysis, n (%)	0	0.0	2	8.0	2.08	1	0.49	
History of PCI, n (%)	8	32.0	8	32.0	0.00	1	1.00	
Biventricular failure, n (%)	9	36.0	19	76.0	8.12	1	0.004	0.40
ICM, n (%)	21	84.0	14	56.0	4.67	1	0.03	-0.31
DCM, n (%)	1	4.0	7	28.0	6.39	1	0.02	0.55
Myocarditis, n (%)	2	8.0	0	0.0	1.40	1	0.49	
Upgrade from Impella CP, n (%)	4	11.8	4	21.1	0.00	1	1.00	
Post-CPR, n (%)	6	24.0	6	24.0	0.00	1	1.00	
Lower INTERMACS profile, n (%)	13	76.5	17	89.5	1.33	1	0.25	
Lactate (mmol/dL)	1.07 ± 0.46		5.20 ± 5.11				0.02	
Bilirubin (mg/dL)	0.88 ± 0.33		2.02 ± 1.57				0.52	

COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; DCM dilatative cardiomyopathy; df, degree of freedom; ICM, ischaemic cardiomyopathy; Impella 5+, Impella 5 or 5.5; INTERMACS, interagency registry for mechanically assisted circulatory support; PCI, percutaneous coronary intervention; phi, phi coefficient; χ^2 , chi-quadrat test. Data documented as n (%) or mean ± standard deviation.

(n = 21). Interestingly, we identified a trend of increased mortality risk for the group with higher INTERMACS profiles (≥ 3) although statistical significance was not reached in this study population. On the other hand, lactate was significantly higher in dead (D) group than in survival (S) group at time of Impella initiation (D vs. S; 5.20 ± 5.11 mg/dL vs. 1.07 ± 0.46 mg/dL, $P = 0.02$).

Subcohort analyses

Because of the heterogeneity of the patient cohort in this study, we categorized our entire cohort into featured subgroups. First, we removed all three cases in the 'planned peri-operative support' (Group 3) from our whole cohort because these cases were hardly comparable with other cases. Thus, 47 cases remained in this subcohort analysis.

"Solo" Impella patients and ECMELLA patients

In 47 cases, we performed subcohort analyses regarding the method of Impella use: the utilization of single 'solo' Impella or ECMELLA (Figure 3). Interestingly, mortality was comparable in both subgroups ('solo' vs. ECMELLA: 55.6% vs. 52.6%, $P = 1.00$). In both subgroups, RVF did not statistically influence mortality (RVF: $P = 0.17$ in the 'solo' group; $P = 0.31$ in the ECMELLA group), but it might have been a risk factor for mortality in both groups if the cohort size were larger. In fact, all three patients with RVF died in the 'solo' Impella group.

In our institute, we initially performed va-ECMO implantation as a standard therapy for acute CS patients, for example,

cardiopulmonary resuscitation (CPR) patients, because of its convenience profile. Figure 4 shows the clinical outcomes depending on the therapeutic concept with or without CPR in patients with ECMELLA. Notably, the 30 day survival rate was comparable in the ECMELLA groups with or without CPR (with CPR vs. without CPR: 50.0% vs. 46.2%, respectively, $P = 1.00$).

Simultaneous utilization of Impella 5+ and TandemHeart

As described, TandemHeart was used in six cases in this study. However, one case required 'solo' TandemHeart for post-operative management of LVAD implantation. In the remaining five cases, the purpose of TandemHeart use was weaning from va-ECMO with support of Impella 5+, in which va-ECMO was successfully removed in all cases. Impella 5+, as well as TandemHeart, were also explanted at a mean of 8.80 ± 7.12 and 15.0 ± 9.0 days after va-ECMO explantation, respectively. The 30 day survival of five patients was 100%, whereas one patient who had CS 4 years post-oHTX died on post-operative day 210 due to septic shock.

Impella 5+ as bridge to permanent mechanical circulatory support

As described, permanent MCS (pMCS) was initiated in six patients (12.8%) via LVAD implantation, with 66.7% of the patients requiring additional tRVAD implantation, while two patients (4.3%) received oHTX. Including the other two patients who underwent direct oHTX on Impella 5+ support, a total of eight patients were enrolled in the pMCS/oHTX group (Figure 2, Table 2). The 30 day survival rate was 100% in this group. To identify the effective potential of Impella 5

Figure 3 The flow chart of mortality depending on ‘solo’ Impella use or ECMELLA with focusing on right ventricular failure. ECMELLA, venous–arterial extracorporeal membrane oxygenation (va-ECMO) plus Impella; RVF, right ventricular failure.

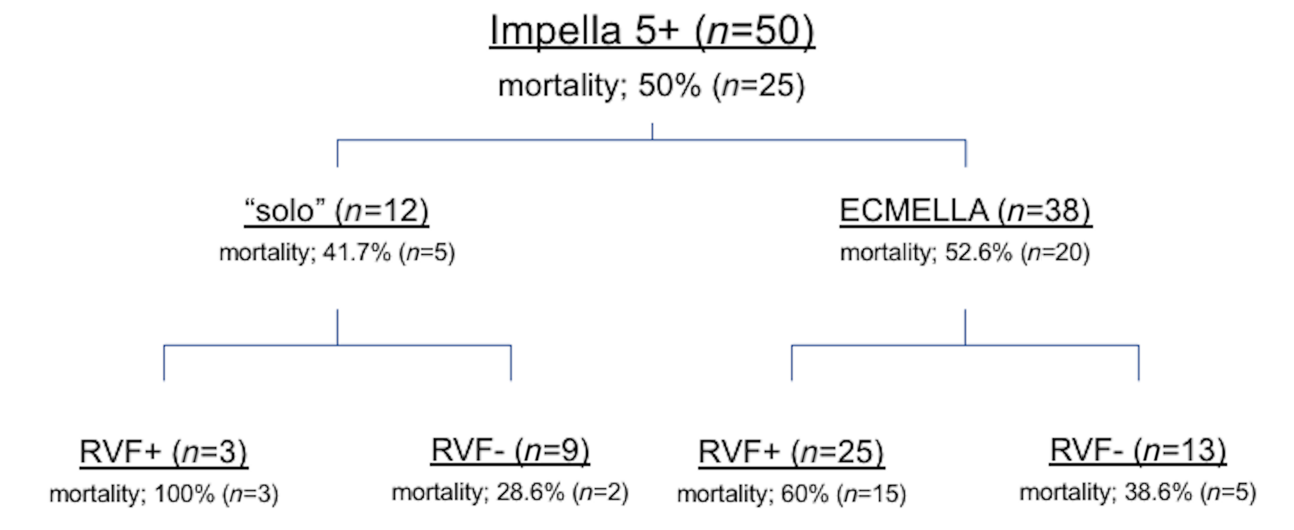
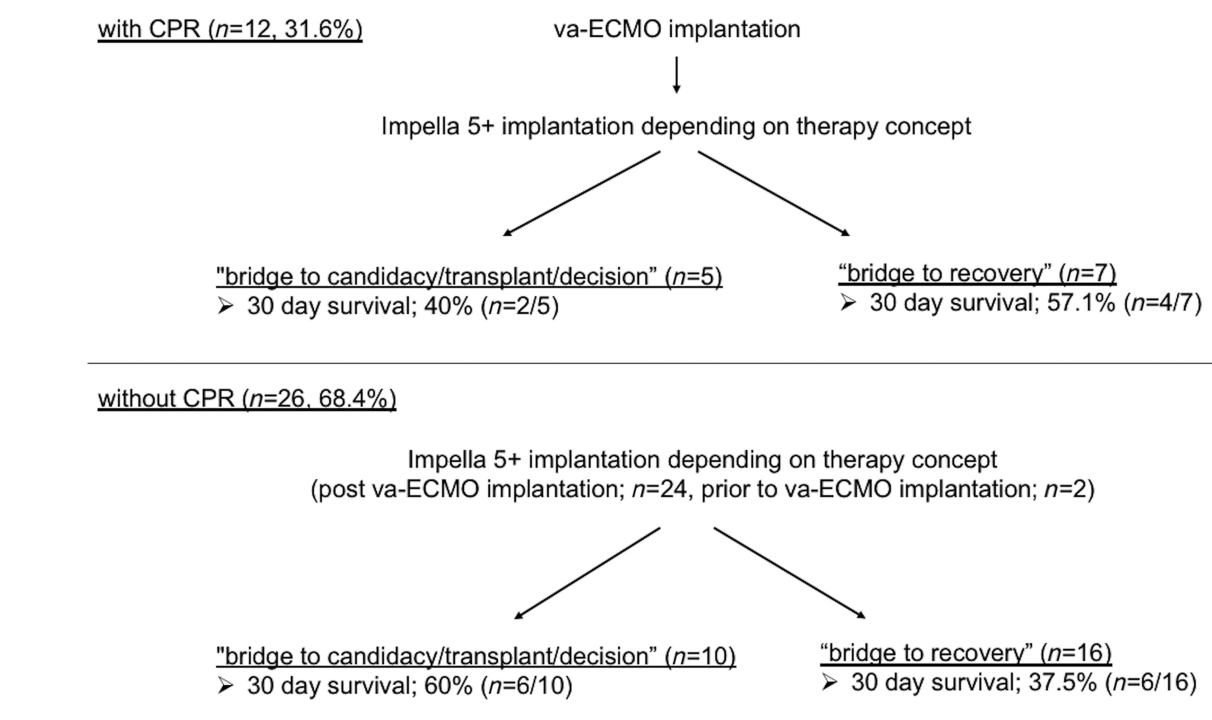


Figure 4 The flow chart of clinical outcome among the 38 ECMELLA cases depending on the therapy concept with or without CPR. CPR, cardiopulmonary resuscitation; ECMELLA, venous–arterial extracorporeal membrane oxygenation (va-ECMO) plus Impella.



+ use as a bridge to pMCS, we compared the patient characteristics between the pMCS/oHTX group ($n = 8$) and the mortality group ($n = 25$). There were no significant differences between both groups regarding patient characteristics; however, pMCS/oHTX patients tended to be younger [55.0 ± 12.5 (vs. 62.5 ± 10.5) years, $P = 0.10$] and with a lower incidence of cardiac surgery leading to LV failure (25.0% vs.

52.0%, $P = 0.24$), whereas biventricular failure indicated no difference between groups (pMCS/oHTX group vs. mortality group: 62.5% vs. 76.0%, respectively, $P = 0.65$). Further, although not statistically significant, there was a trend towards more impaired end-organ function in the mortality group with higher lactate at the time of Impella 5+ initiation (Table 5).

Table 5 Patient characteristics in pMCS/oHTX group and mortality group

	pMCS/oHTX (n = 8)		Mortality (n = 25)		P
Age (years)	55.0 ± 12.5		62.5 ± 10.5		0.10
Biventricular failure, n (%)	5	62.5	19	76.0	0.65
Post-cardiotomy syndrome, n (%)	2	25.0	13	52.0	0.24
Lactate (mmol/dL)	1.93 ± 1.48		4.66 ± 5.62		0.19

oHTX, orthotopic heart transplantation; pMCS, permanent mechanical circulatory support.

Data documented as n (%) or mean ± standard deviation.

Discussion

With the introduction of microaxial pump catheters, such as Impella 5.0 or Impella 5.5, into clinical routine, we face a new era in which fundamentally different concepts of MCS may be used as alternative or additive tools for temporary support of critically ill patients who present with CS. This technical freedom of choice comes with an increase in decision-making complexity with respect to the optimal therapy strategy for individual patients. The clinical evidence in this field is limited, and that concerning Impella 5+ is even scarcer. The main purpose of this study was to analyse our initial 50 cases using Impella 5+ to elucidate factors determining therapy efficacy and patient outcome and to share this experience.

When analysing the risk factors for mortality among patients with Impella support, ICM as an underlying disease provided a statistically significant factor for benign prognosis. We speculate that this effect may be related to the underlying circulatory pathophysiology. Impella support is expected to improve cardiac output, thereby augmenting systemic blood pressure and elevating peripheral circulation, while simultaneous true LV unloading decreases myocardial wall tension, which increases coronary perfusion and reduces pathologically increased LV end-diastolic pressure. In this sense, Impella appears to be a promising treatment strategy that can stabilize haemodynamics while suppressing the increase in myocardial oxygen consumption by unloading the left ventricle in patients with ICM. These modes of action and parts of the underlying mechanisms have already been demonstrated in a number of previous studies.^{5–9} Within the ICM group, a small but yet distinct subcohort, characterized by severe coronary artery disease and concomitant severely depressed LV function, deserves particular consideration. There may be a good reason to perform CABG without cardioplegic arrest in the latter patients to avoid ischaemia reperfusion injury and post-operative CS, which may require rescue MCS with the consecutive risk of various complications. However, the beating heart coronary bypass operation is technically challenging and particularly demanding in the context of severely depressed function and markedly enlarged dimensions of the LV. In this study, we also present successful Impella-supported beating heart CABG with planned Impella 5.0 implantation for circulatory support in

the setting of severely depressed LV function. All three patients recovered well and demonstrated improved LVEF and LVEDD at the time of hospital discharge. Some previous case series have indicated the utility and potential benefit of Impella in supporting bypass operations.^{10–13} However, there is still no randomized trial to identify the usefulness of concomitant Impella 5+ implantation as circulatory support for beating heart CABG. According to our clinical results, we suppose that across the real-world spectrum of Impella 5+ utilization, this particular indication (i.e. Impella-supported beating heart CABG in high-risk patients) may represent a favourable strategy. On the other hand, our results confirm previous findings suggesting that biventricular failure, for example, DCM, is a predictor of increased mortality in patients with CS.¹⁴ We observed a statistically and clinically significant effect with inferior outcomes in patients with DCM as the underlying cause of CS. On the first glance, this finding may be explained by the fact that the use of Impella, which is primarily a left-sided mechanical support device, may not be sufficient to significantly influence the better clinical outcomes for patients with evident biventricular failure. Despite the statistical difference evident in this study, we believe that due to the relatively limited sample size of this subcohort, the impact of DCM on the outcome of patients with CS supported by Impella will have to be analysed in larger studies.

In life-threatening conditions, such as ongoing CPR or refractory arrhythmia, peripheral va-ECMO often remains the first choice for rapid and confirmed establishment of systemic circulation. The support of va-ECMO contributes to the increase in blood pressure, but it also increases the LV end-diastolic volume and promotes a shifting of the PV loop to the right, which leads to pulmonary congestion.¹⁵ Therefore, concomitant Impella implantation, ECMELLA, is a treatment option that not only stabilizes haemodynamics, but also unloads the left ventricle, thereby decreasing wall tension and myocardial oxygen consumption.¹⁶ Vallabhajosyula *et al.* reported in their review article that the use of Impella was associated with a higher weaning rate from va-ECMO and bridging to destination therapy, such as LVAD implantation or oHTX.¹⁷ Patel *et al.* found in their study that ECMELLA had a higher survival rate after 30 days, a lower rate of catecholamine use, and was as safe as va-ECMO alone.¹⁸ In our study, the in-hospital mortality of all patients with ECMELLA was 47.4% (n = 18/38). Considering the risk profile in this

cohort, we regard this result as acceptable. Further, we observed an interesting result in subcohort analyses; the mortality was comparable between the 'solo' Impella and ECMELLA groups, despite the severity of the patients in the ECMELLA group, requiring 33.3% post-CPR. This indicates the effective use of a large Impella system in va-ECMO.

On the other hand, tRVAD, such as TandemHeart, often becomes necessary for successful MCS therapy; however, previous reports have noted a persistently worse prognosis irrespective of the use of tRVAD in this setting.^{14,19} In contrast, our study demonstrated an impressive result of tRVAD (30 day survival 100%, $n = 9/9$, in-hospital mortality 11.1%, $n = 1/9$). Of note, tRVAD was directly implanted after Impella explantation and LVAD implantation in four patients, that is, during the same operation. In the other five patients, however, tRVAD was implanted with a certain delay after the initial ECMO implantation. In these cases, tRVAD was implanted with the intention of facilitating weaning of the va-ECMO. Nevertheless, one of the latter patients died from multiple organ failure due to septic shock on post-operative day 210. Impella implantation with consideration of concomitant RVAD implantation will be another relevant topic of therapy strategy for biventricular failure patients. We believe that the use of biventricular percutaneous MCS, for example Impella 5+ combined with tRVAD (e.g. TandemHeart), would be an ideal therapy strategy to wean patients from va-ECMO early after prior emergency implantation.

In the present cohort, we observed an overall 30 day survival rate of 56.0%; half of all patients treated with Impella 5+ experienced in-hospital mortality. We regard this result as an acceptable outcome considering the high proportion of critically ill patients, with a considerable fraction of patients presenting with biventricular failure or INTERMACS Profiles 1 or 2. Concerning key factors for successful transition to pMCS (i.e. permanent LVAD or oHTX) interestingly, biventricular failure indicated no impact, whereas younger age, absence of signs of post-cardiotomy syndrome, and preserved end-organ function seemed to be factors with a positive impact on successful transition to pMCS or oHTX, although we could not achieve statistical significance in the present cohort.

This study had several limitations. First, this report represents a retrospective analysis of non-randomized patients with a limited cohort size from a single centre. Potential systemic measurement errors and factors can influence the outcomes. Second, our analysis does not cover data on long-term outcomes; therefore, the prognostic factors described herein are limited to short-term outcomes. Long-term

follow-up may provide novel insights into the lasting benefits of microaxial pump therapy for patients with severely depressed LV function. Third, our data did not allow for a comparative study evaluating the size of the Impella pump (CP vs. 5.0 or 5.5). This analysis will let us indicate the optimal timing of large Impella utilisation. Further studies, especially multicentre randomized studies, are warranted to confirm our therapeutic strategy in CS patients.

Conclusion

In a consecutive series of all-comer patients with CS, temporary MCS via Impella 5+ (Impella 5.0 or 5.5) seemed to be a promising strategy to improve outcomes, with a particular benefit in ICM patients. A superior outcome may be accessible by planned Impella 5+ support in preparation for bypass surgery without the use of a heart lung machine in the setting of severely depressed LV function. In contrast, the survival rate and overall outcome were inferior for patients with biventricular failure requiring MCS. ECMELLA therapy might be effective for better prognosis, and the use of Impella 5+ combined with tRVAD is a promising strategy for early weaning from va-ECMO. Further clinical evaluation is needed to generate solid evidence regarding the role of microaxial pump therapy in patients requiring MCS.

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Conflict of interest

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