

Unprotected versus protected high-risk percutaneous coronary intervention with the Impella 2.5 in patients with multivessel disease and severely reduced left ventricular function

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Abstract

Selecting a revascularization strategy in patients with multivessel disease (MVD) and severely reduced left ventricular ejection fraction (LVEF) remains a challenge. PCI with Impella 2.5 may facilitate high-risk PCI, however long-term results comparing unprotected versus protected PCI are currently unknown. We sought to evaluate the outcome of patients undergoing protected compared to unprotected percutaneous coronary intervention (PCI) in the setting of MVD and severely reduced LVEF.

We included patients with MVD and severely reduced LVEF ($\leq 35\%$) in this retrospective, single-centre study. Patients that underwent unprotected PCI before the start of a dedicated protected PCI program with Impella 2.5 were compared to patients that were treated with protected PCI after the start of the program. The primary endpoint was defined as major adverse cardiac and cerebrovascular events (MACCE) during a 1-year follow-up. The secondary endpoints consisted of in-hospital MACCE and adverse events.

A total of 61 patients (mean age 70.7 ± 10.9 years, 83.6% male) were included in our study, of which 28 (45.9%) underwent protected PCI. The primary endpoint was reached by 26.7% and did not differ between groups ($P = .90$). In-hospital MACCE ($P = 1.00$) and in-hospital adverse events ($P = .12$) also demonstrated no significant differences. Multivariate logistic regression identified procedural success defined as complete revascularization and absence of in-hospital major clinical complications as protective parameter for MACCE (OR 0.17, 95% CI 0.04–0.70, $P = .02$).

Patients with MVD and severely depressed LVEF undergoing protected PCI with Impella 2.5 demonstrate similar in-hospital and one-year outcomes compared to unprotected PCI.

Abbreviations: AKI = acute kidney injury, CKD = chronic kidney disease, LVEF = left ventricular ejection fraction, MACCE = major adverse cardiac and cerebrovascular events, MVD = multivessel disease, PCI = percutaneous coronary intervention.

Keywords: high-risk PCI, Impella, multivessel disease, peripheral ventricular assist devices, protected PCI

1. Introduction

Determining the optimal revascularization strategy in patients with coronary multivessel disease (MVD) and severely reduced left ventricular ejection fraction (LVEF) remains a clinical challenge. Current guidelines issued by the European Society of Cardiology (ESC) and the American Heart Association (AHA)

base the decision whether to recommend percutaneous coronary intervention (PCI) or coronary artery bypass grafting on a careful assessment of the complexity of coronary artery disease in consideration of the patient's individual characteristics and procedural risk.^[1–3] The continuing evolution of catheter techniques and materials allows for the treatment of ever more complex coronary artery disease by PCI. At the same time, the demographic development accounts for older patients with an increasing number of comorbidities, translating into a higher frequency of high-risk PCIs.^[4]

High-risk PCI may result in hypotension, compromised cardiac perfusion, the development of cardiogenic shock and cardiac arrest.^[5,6] Patients featuring severe coronary artery disease and reduced LVEF are particularly prone to peri-procedural complications and exhibit poorer long-term outcomes.^[6–8] In this subset of patients, the temporary implantation of a peripheral ventricular assist device may improve short- and long-term outcomes.^[9,10]

The Impella 2.5 is a coaxial miniaturized rotary blood pump that supports the left ventricle with up to 2.5 L/min of blood flow and may secure coronary and systemic perfusion.^[11–13] The PROTECT-I trial demonstrated the feasibility and safety of the protected PCI approach with the Impella 2.5 device, while the PROTECT-II trial showed superior hemodynamic support and a strong trend toward lower rates of major adverse cardiac and cerebrovascular events (MACCE) at 3-month follow-up compared to the intraaortic balloon pump.^[12,13] These results were

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confirmed in a real-world clinical setting in the USpella Registry.^[14] Impella 2.5 support could further exert a protective effect against acute kidney injury (AKI) during high-risk PCI.^[15]

We have previously reported that patients with MVD undergoing protected PCI with the Impella 2.5 device experience similar in-hospital outcomes when compared to coronary artery bypass grafting.^[16] However, there are currently no data available comparing in-hospital and long-term outcomes of patients undergoing Impella 2.5-supported PCI with unprotected PCI.

The aim of the present study was to evaluate outcomes of patients undergoing PCI before and after the implementation of a dedicated protected PCI program using the Impella 2.5 in the setting of MVD and severely reduced LVEF.

2. Methods

2.1. Study design

This study was designed as an observational, retrospective single-centre study. A dedicated “protected PCI program” using the Impella 2.5 (Abiomed, Danvers, MA) was implemented in our tertiary care institution in October 2015. The program featured extensive training of involved personnel, the establishment of standard operational procedures for patient selection and treatment as well as follow-up of patients. In this study, we consecutively included patients presenting with MVD and severely reduced LVEF undergoing protected PCI supported by Impella 2.5 in a 12-month period of time after the implementation. This cohort was compared with consecutive patients with MVD and severely reduced LVEF undergoing unprotected PCI without percutaneous left ventricular assist device in a 12-month period before the implementation of the program.

MVD was defined as the presence of $\geq 75\%$ luminal diameter stenosis in 2 or more major epicardial coronary arteries or the presence of $\geq 50\%$ luminal diameter stenosis of the left main trunk. Severely reduced LVEF was defined as LVEF below or equal to 35% as evaluated by echocardiography before intervention.

Patients suffering from cardiogenic shock before intervention, defined as hypotension with systolic blood pressure < 90 mm Hg for > 30 minutes or the need for supportive measures to maintain a systolic blood pressure above or equal to 90 mm Hg were excluded.

The study was carried out according to the principles of the declaration of Helsinki and was approved by the Medical Ethics Commission II of the Faculty of Medicine Mannheim, University of Heidelberg, Germany (Ethical-approval-no. 2016-862R-MA). The need for informed consent was waived due to the retrospective design of the study.

2.2. Patient population

In patients with an elective indication, the revascularization strategy was determined by an interdisciplinary heart team consisting of an interventional cardiologist, a cardiac surgeon and a cardiac anesthetist taking into consideration the individual patient's preference. In patients with acute coronary syndrome, the mode of revascularization was determined by an experienced interventional cardiologist.

With the start of the “protected PCI program” in October 2015, 2 experienced interventional cardiologists assessed all patients selected for PCI in terms of patient-specific and lesion-specific properties that predict an increased periprocedural risk

according to the 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care.^[17] Only patients, in whom both PCI were considered the primary choice of revascularization and protected PCI was recommended and feasible were included in our study. All patients included in the study that underwent unprotected PCI before the implementation of the “protected PCI program” were retrospectively assessed using the same principals described above and would have also been eligible for the treatment with protected PCI. The complete inclusion process is demonstrated in Fig. 1.

2.3. Percutaneous coronary intervention

In both study arms, PCI was performed according to current societal guidelines and at the discretion of the treating interventional cardiologist.^[2] In all patients, PCI was carried out with the goal of complete revascularization. Each patient in this study received echocardiography before the intervention to evaluate LVEF and to exclude severe aortic stenosis rendering the implantation of the Impella device impossible.

2.4. Protected PCI with the Impella 2.5 device

Duplex sonography was performed prior the implantation to exclude relevant peripheral vascular disease. The common femoral artery was punctured and a 13-F femoral sheath was inserted after dilatation using the provided set. A preclose technique was used to facilitate sheath removal by inserting 2 6F Perclose Proglide (Abbott Vascular Santa Clara, CA) devices before placing the vascular sheath. The Impella 2.5 was inserted into the left ventricle under fluoroscopic guidance using a pigtail catheter followed by a 0.018-inch guide wire on which Impella device was advanced so that the outlet area of the axial pump rested above the aortic valve. The automated Impella controller in combination with fluoroscopy was used to assess the correct device position after the removal of the guidewire. The device was left in place during the procedure and was explanted after guide removal. If determined necessary by the treating interventional cardiologist, the Impella 2.5 was left in place for a maximum of 24 hours after the intervention. Procedural duration was measured after the implantation of the Impella device starting with the placement of the guide catheter and ending with vessel closure.

2.5. Procedural outcomes

Procedural outcomes were defined according to 2011 ACCF/AHA/SCAI Guideline for PCI.^[2] Residual stenosis was defined as incomplete revascularization of a coronary segment with a luminal diameter stenosis $\geq 75\%$ or $\geq 50\%$ for the left main trunk respectively. Revascularization was considered incomplete if a stenosis of 10% or more remained after stenting and patients without residual stenosis after intervention were classified as angiographic success.^[2] Procedural success was defined as angiographic success without associated in-hospital major clinical complications.^[2]

2.6. Primary endpoints

The primary endpoint of this study was defined as MACCE during a one-year follow-up period. MACCE consisted of cardiovascular mortality, myocardial infarction, repeat target vessel revascularization (both coronary artery bypass grafting

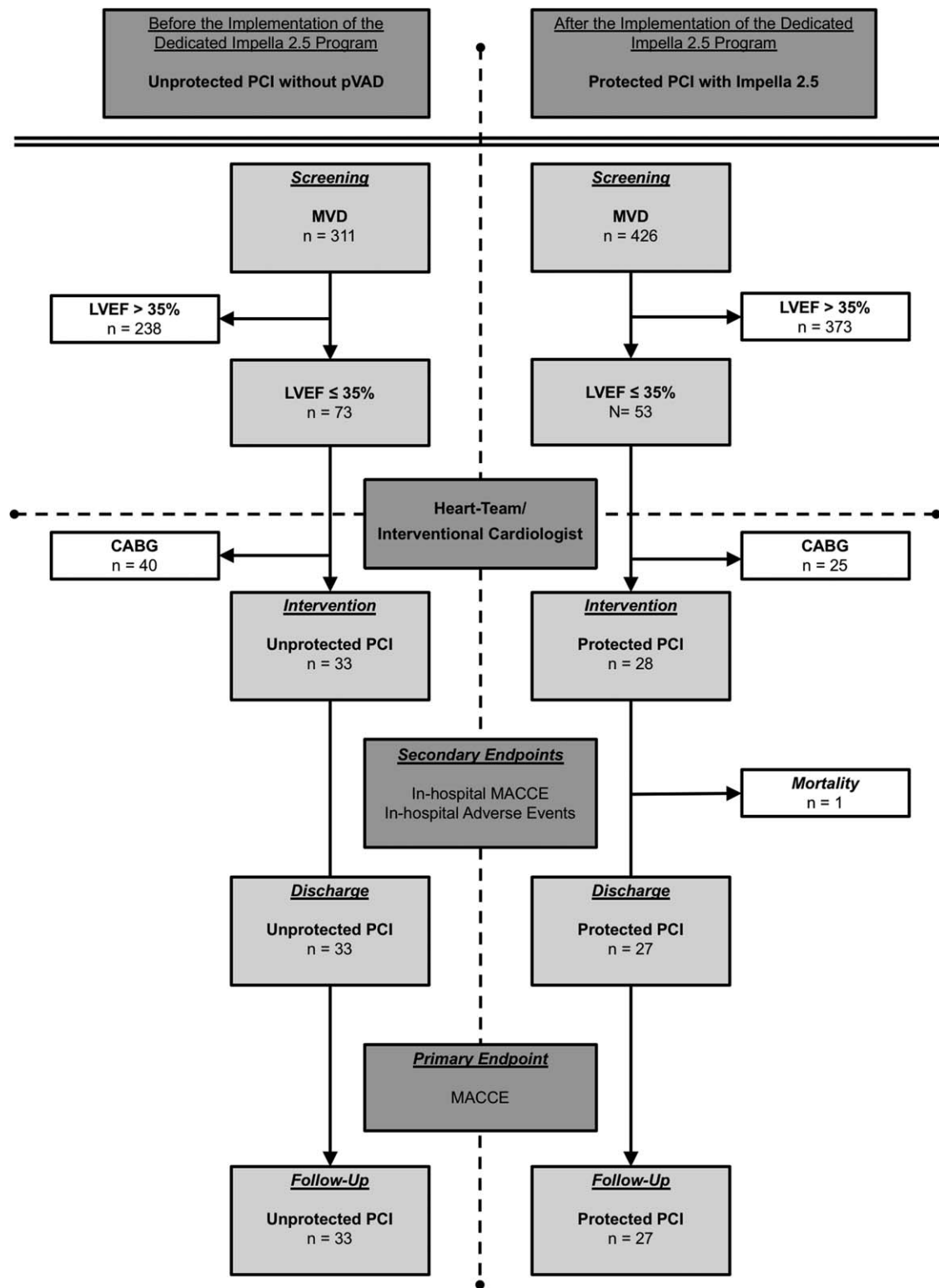


Figure 1. Study design. CABG=coronary artery bypass grafting, LVEF=left ventricular ejection fraction, MACCE=major adverse cardiac and cerebrovascular event, MVD=multivessel disease, PCI=percutaneous coronary intervention, pVAD=percutaneous ventricular assist device.

and PCI) and stroke. Cardiovascular mortality was defined as death attributable to acute myocardial infarction, sudden cardiac death, heart failure, stroke, cardiovascular procedure or hemorrhage and other cardiovascular causes.^[18] Myocardial infarction was defined as elevation of troponin or CK-MB both

above of 2 times the upper limit of the reference range used by the local laboratory. Laboratory changes must occur in combination with ischemic symptoms or development of pathologic Q-waves or ST segment changes on electrocardiography. Repeat revascularization was defined as repeat intervention that involved the

target lesion, target or nontarget vessels, performed either by PCI or coronary artery bypass grafting. Stroke was defined as permanent (longer than 24 hours), focal or global neurological deficits ascertained by a standard neurological examination and evidence of ischemia on an imaging study.

2.7. Secondary endpoints

The secondary endpoint consisted of in-hospital MACCE and in-hospital adverse events. In-hospital adverse events were defined as a combination of both peri- and postprocedural complications including cardiac arrhythmia and/or cardiopulmonary resuscitation, AKI, dissection of a coronary or the aorta, cardiac or vascular operation as well as pulmonary edema, pericardial effusion, cardiogenic shock or the need for an additional left ventricular assist device. Cardiac arrhythmia was defined as a sustained ventricular tachycardia, ventricular fibrillation or atrial fibrillation requiring cardioversion or cardiopulmonary resuscitation. AKI was defined according to 2012 KDIGO clinical practice guideline for AKI and staged for severity by AKIN-criteria.^[19] AKI stage 1 was defined as a rise in serum creatinine of ≥ 0.3 mg/dL or 1.5 to 1.9 times baseline and stage 2 as 2.0 to 2.9 times increase of serum-creatinine from baseline. AKI stage 3 was defined as an increase of ≥ 3.0 times from baseline or serum-creatinine >4.0 mg/dL with an acute increase of >0.5 mg/dL or the indication for dialysis or hemofiltration during hospital stay. Cardiac or vascular operation was defined as any cardiac or thoracic, abdominal vascular or vascular surgery. Clinical baseline characteristics and medical data were collected from medical reports and were recorded in electronic chart review form in an electronic data capturing system.

2.8. Follow-up

One-year follow-up was conducted via telephone interview using a structured questionnaire or a clinical follow-up in our outpatient clinic. In-hospital MACCE and in-hospital adverse events were assessed by chart review.

2.9. Statistical analysis

The statistical analysis was performed using SAS (Version 9.04, SAS Institute, Inc., Cary, NC) and as intention-to-treat analysis. Data are presented as means \pm standard deviation for continuous variables with a normal distribution, median with interquartile range for continuous variables with a nonnormal distribution, and as frequency for categorical variables. The Kolmogorov–Smirnov test was used to assess normal distribution. Student *t* test and the Mann–Whitney *U* test were used to compare continuous variables with normal and nonnormal distributions, respectively. The Chi-squared test or Fisher exact test was used to compare categorical variables. To examine predictors of the primary endpoint of MACCE, univariate and multivariate logistic regression were conducted. All predictor variables significant at a 2-tailed *P*-value of $<.1$ were then entered into the multivariate logistic regression model to adjust for potential confounders. A 2-tailed *P*-value of $<.05$ was considered statistically significant in all tests.

3. Results

3.1. Patient characteristics

A total of 61 patients (70.7 ± 10.9 years, 83.6% male) were included in our study. Twenty-eight patients (45.9%) underwent

protected PCI with the Impella 2.5 while 33 patients (54.1%) received unprotected PCI. Significantly more patients were male in the protected compared to the unprotected PCI group (96.4% vs 72.7%, $P < .05$). Mean LVEF did not show a statistically significant difference between groups (28.1% vs 30.9%, $P = .09$). Patients treated with protected PCI demonstrated a significantly higher mean SYNTAX score (33.3 ± 10.6 vs 24.3 ± 14.7 , $P < .01$) while patients that underwent unprotected PCI presented with a significantly higher mean EuroScore II ($9.4 \pm 7.3\%$ vs $5.0 \pm 4.7\%$, $P < .01$). There were no statistically significant differences concerning NYHA-class upon admission ($P = .59$) and number of patients presenting with angina pectoris CCS III or higher ($P = .31$) between both groups.

Indications for PCI were similar in both groups and there was no difference between elective indications and acute coronary syndrome (both $P = .43$). Prior coronary artery bypass grafting was more prevalent in patients that underwent protected PCI (17.9% vs 0.0%, $P < .05$). The prevalence of chronic kidney disease (CKD) was distributed similar between the groups ($P = .70$). Severe CKD defined as baseline glomerular filtration rate lower than 30 mL/min/1.73 m² was significantly higher in the protected PCI group (18.5% vs 0.0%, $P < .05$). The mean number of vessels involved per patient (3.3 ± 0.6 vessels vs 2.4 ± 0.7 vessels, $P < .001$) as well as mean number of involved coronary segments (7.3 ± 2.6 segments vs 4.0 ± 2.6 segments, $P < .001$) was also significantly higher in patients treated with protected PCI. Patient characteristics are demonstrated in Table 1.

3.2. Procedural characteristics

Implantation of the Impella 2.5 was successful in 27 patients (96.4%) and vascular access for the device was exclusively gained via the A. femoralis. In one case, advancement of the Impella 2.5 beyond the aortic valve was not possible. Twenty-five (92.6%) patients in the protected PCI group received Impella 2.5 support for the intervention only, while prolonged postprocedural support was necessary in 2 patients (7.4%). Protected PCI patients were treated with a significantly higher mean number of stents per patient (4.6 ± 2.2 stents vs 3.0 ± 1.4 stents, $P < .01$). This translated into a higher mean stent length in the protected PCI group (110.6 ± 59.7 mm vs 56.7 ± 30.3 mm, $P < .001$). Although not statistically significant, patients who underwent protected PCI demonstrated a lower rate of residual stenosis (17.9% vs 33.3%, $P = .17$), which resulted in a numerical higher percentage of angiographic (82.1% vs 66.7%, $P = .17$) and procedural success (78.6% vs 66.7%, $P = .30$). Procedural characteristics for both groups are demonstrated in Table 2.

3.3. Primary endpoint

The primary endpoint occurred in 16 patients (26.7%) with no statistically significant differences between groups ($P = .90$). Cardiovascular mortality was numerically higher in the protected PCI group but did not reach statistical significance (22.2% vs 9.1%, $P = .28$). The occurrences of myocardial infarction (14.8% vs 6.5%, $P = .40$), repeat revascularization (7.4% vs 16.1%, $P = .43$), and stroke (0.0% vs 3.2%, $P = 1.00$) were also distributed evenly between the groups. MACCE rates are demonstrated in Table 3.

After adjusting for variables that demonstrated an impact on long-term MACCE in a univariate regression model, procedural success remained as single protective parameter in

Table 1**Patient characteristics.**

	All, n=61 (100%)	Protected PCI with Impella 2.5, n=28 (45.9%)	Unprotected PCI, n=33 (54.1%)	P
Age, mean±SD	70.7±10.9	71.2±11.0	70.3±11.0	.75
Male sex, n (%)	51 (83.6%)	27 (96.4%)	24 (72.7%)	<.05
Left ventricular ejection fraction, mean±SD	29.4±6.5	30.9±6.0	28.1±6.7	.09
Duration of hospital stay in days, median (IQR)	6.0 (3.0-11.0)	4.5 (3.0-11.0)	6.0 (2.0-12.0)	.86
Indication for PCI, n (%)				
Acute coronary syndrome	36 (59.0%)	15 (53.6%)	21 (63.6%)	.43
Elective procedure	25 (41.0%)	13 (46.4%)	12 (36.4%)	.43
Cardiovascular risk factors, n (%)				
Hypertension	48 (78.7%)	20 (71.4%)	28 (84.8%)	.20
Hypertlipidemia	48 (78.7%)	27 (96.4%)	21 (63.6%)	<.01
Smoker	27 (44.3%)	12 (42.9%)	15 (45.5%)	.84
Diabetes mellitus	23 (37.7%)	12 (42.9%)	11 (33.3%)	.44
IDDM	8 (13.1%)	3 (10.7%)	5 (15.2%)	.72
NIDDM	15 (24.6%)	9 (32.1%)	6 (18.2%)	.21
Chronic kidney disease*	19 (32.2%)	8 (29.6%)	11 (34.4%)	.70
Mild (GFR 45–59 mL/min/1.73 m ²)	10 (16.9%)	3 (11.1%)	7 (21.9%)	.32
Moderate (GFR 30–44 mL/min/1.73 m ²)	4 (6.8%)	0 (0.0%)	4 (12.5%)	.12
Severe (GFR <30 mL/min/1.73 m ²)	5 (8.5%)	5 (18.5%)	0 (0.0%)	<.05
Cardiovascular history, n (%)				
Coronary artery disease	35 (57.4%)	17 (60.7%)	18 (54.5%)	.63
Prior myocardial infarction	23 (37.7%)	9 (32.1%)	14 (42.4%)	.41
Prior PCI	32 (52.5%)	15 (53.6%)	17 (51.5%)	.87
Prior CABG	5 (8.2%)	5 (17.9%)	0 (0.0%)	<.05
Peripheral vascular disease	7 (11.5%)	5 (17.9%)	2 (6.1%)	.23
Atrial fibrillation	13 (21.3%)	7 (25.0%)	6 (18.2%)	.52
Involved major coronary arteries				
Number of vessels involved, mean±SD	2.8±0.8	3.3±0.6	2.4±0.7	<.001
Left main trunk [†] , n (%)	25 (41.0%)	15 (53.6%)	10 (30.3%)	.07
Left anterior descending artery [‡] , n (%)	50 (82.0%)	26 (92.9%)	24 (72.7%)	<.05
Left circumflex artery [‡] , n (%)	55 (90.2%)	27 (96.4%)	28 (84.8%)	.20
Right coronary artery [‡] , n (%)	40 (65.6%)	23 (82.1%)	17 (51.5%)	<.05
Number of involved coronary segments, mean±SD [§]	5.5±3.0	7.3±2.6	4.0±2.6	<.001
Risk classification				
Current NYHA-class III or IV, n (%)	24 (39.3%)	10 (35.7%)	14 (42.4%)	.59
Current CCS III or IV, n (%)	26 (42.6%)	10 (35.7%)	16 (48.5%)	.31
EuroSCORE II, mean±SD	7.4±6.6	5.0±4.7	9.4±7.3	<.01
SYNTAX I score, mean±SD	28.4±13.7	33.3±10.6	24.3±14.7	<.01

CABG=coronary artery bypass grafting, GFR=glomerular filtration rate, IDDM=insulin-dependent diabetes mellitus, IQR=interquartile range, NIDDM=noninsulin-dependent diabetes mellitus, PCI=percutaneous coronary intervention, SD=standard deviation.

* Baseline GFR <60 mL/min/1.73 m².

[†] Luminal diameter stenosis ≥50%.

[‡] Luminal diameter stenosis ≥75%.

[§] Coronary segments with luminal diameter stenosis ≥75%, left main trunk ≥50%.

the multivariate model (OR 0.17, 95% CI 0.04–0.76, $P=.02$). Increased age (OR 2.40 per decade, 95% CI 1.18–4.89, $P=.02$) was associated with an increased risk of MACCE while procedural duration (OR 1.28, 95% CI 1.00–1.64, $P=.05$) showed a strong trend toward worse outcomes in the multivariate model. Of note, Impella support did not impact MACCE in the univariate model (OR 1.33, 95% CI 0.44–4.04, $P=.61$). Regression analysis is demonstrated in Table 4 and Fig. 2.

3.4. Secondary endpoints

The secondary endpoint of in-hospital MACCE (3.6% vs 3.0%, $P=1.00$) as well as in-hospital adverse events (39.3% vs 21.2%, $P=.12$) did not differ significantly between both groups. The rates of cardiac arrhythmia and/or cardiopulmonary resuscitation, dissection of a coronary artery or the aorta as well as pulmonary

edema were similar between both groups (all $P=1.00$). Of note, the rate of postprocedural AKI was also similar between groups (32.1% vs 18.2%, $P=.20$). Adverse events including cardiogenic shock, the need for an additional left ventricular assist device, cardiac or vascular surgery and pericardial effusion did not occur in our study. Secondary endpoints are listed in Table 3.

4. Discussion

Our study evaluated the outcome of patients with MVD and severely depressed LVEF undergoing unprotected PCI or protected PCI with the Impella 2.5. To date, only few randomized, controlled trials have been conducted with the Impella device.^[13,20–22] All employed intraaortic balloon pump treatment as a control group, and there are currently no randomized controlled trials available that directly compare

Table 2

Procedural characteristics.

	All, n = 61 (100%)	Protected PCI with Impella 2.5, n = 28 (45.9%)	Unprotected PCI, n = 33 (54.1%)	P
Vascular access via A. femoralis, n (%)	48 (78.7%)	28 (100%)	20 (60.6%)	<.001
Vascular access via A. radialis, n (%)	13 (21.3%)	0 (0.0%)	13 (39.4%)	<.001
Closure device, n (%)	36 (59.0%)	22 (78.6%)	14 (42.4%)	<.01
Mean procedure time, min	68.4 ± 28.9	77.3 ± 31.0	60.8 ± 24.9	.05
Mean contrast volume, mL	229.1 ± 86.8	227.3 ± 99.8	230.7 ± 75.7	.43
Stent characteristic				
Total number of stents implanted, n	228	128	100	.06
Mean number of stents implanted per patient	3.7 ± 2.0	4.6 ± 2.2	3.0 ± 1.4	<.01
Mean stent length per patient, mm	81.9 ± 53.4	110.6 ± 59.7	56.7 ± 30.3	<.001
1st Generation DES, n (%)				
Paclitaxel-eluting stent	6 (2.6%)	1 (0.8%)	5 (5.0%)	.71
Sirolimus-eluting stent	5 (2.2%)	0 (0.0%)	5 (5.0%)	—
Sirolimus-eluting stent	1 (0.4%)	1 (0.8%)	0 (0.0%)	—
2nd Generation DES, n (%)				
Everolimus-eluting stent	218 (95.6%)	123 (96.1%)	95 (95.0%)	.07
Everolimus-eluting stent	191 (83.8%)	123 (96.1%)	68 (68.0%)	—
Zotarolimus-eluting stent	27 (11.8%)	0 (0.0%)	27 (27.0%)	—
3rd Generation DES, n (%)				
Biolimus-eluting stent	4 (1.8%)	4 (3.1%)	0 (0.0%)	.46
Biolimus-eluting stent	4 (1.8%)	4 (3.1%)	0 (0.0%)	—
Impella characteristics, n (%)				
Vascular access for Impella 2.5 via A. femoralis		28 (100%)		
Successful implantation of Impella 2.5		27 (96.4%)		
Periprocedural support only		25 (92.6%)		
Prolonged postprocedural support ≤24 h		2 (7.4%)		
Procedural results, n (%)				
Procedural success	44 (72.1%)	22 (78.6%)	22 (66.7%)	.30
Angiographic success	45 (73.8%)	23 (82.1%)	22 (66.7%)	.17
Residual stenosis	16 (26.2%)	5 (17.9%)	11 (33.3%)	.17

Unless otherwise specified, data are means ± SD.

DES=drug-eluting stent, PCI=percutaneous coronary intervention, SD=standard deviation.

protected and unprotected PCI. This illustrates the conceptual and ethical challenges when comparing the 2 patient groups prospectively and underlines the importance of retrospective, observational studies to elucidate the efficiency of the protected PCI approach with the Impella 2.5. We demonstrate that Impella-

2.5-protected PCI in high-risk patients yields comparable results to patients undergoing unprotected PCI in terms of in-hospital and long-term MACCE.

MACCE rates reported in our study are comparable to prior trials that examined protected PCI with the Impella

Table 3

Primary and secondary endpoints.

	All, n = 61 (100%)	Protected PCI with Impella 2.5, n = 28 (45.9%)	Unprotected PCI, n = 33 (54.1%)	P
MACCE				
Cardiovascular mortality	16 (26.7%)	7 (25.9%)	9 (27.3%)	.90
Myocardial infarction	9 (15.0%)	6 (22.2%)	3 (9.1%)	.28
Myocardial infarction	6 (10.3%)	4 (14.8%)	2 (6.5%)	.40
Repeat revascularization	7 (12.1%)	2 (7.4%)	5 (16.1%)	.43
Stroke	1 (1.7%)	0 (0.0%)	1 (3.2%)	1.00
Secondary endpoints, n (%)				
In-hospital MACCE				
Cardiovascular mortality	2 (3.3%)	1 (3.6%)	1 (3.0%)	1.00
Cardiovascular mortality	1 (1.6%)	1 (3.6%)	0 (0.0%)	.46
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
Repeat revascularization	1 (1.6%)	0 (0.0%)	1 (3.0%)	1.00
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
In-hospital adverse events				
Acute kidney injury	18 (29.5%)	11 (39.3%)	7 (21.2%)	.12
Acute kidney injury	15 (24.6%)	9 (32.1%)	6 (18.2%)	.20
AKI stage 1	10 (16.4%)	5 (17.9%)	5 (15.2%)	1.00
AKI stage 2	1 (1.6%)	1 (3.6%)	0 (0.0%)	.46
AKI stage 3	4 (6.6%)	3 (10.7%)	1 (3.0%)	.32
Cardiac arrhythmia and/or CPR	5 (8.2%)	2 (7.1%)	3 (9.1%)	1.00
Dissection of coronary artery or aorta	1 (1.6%)	0 (0.0%)	1 (3.0%)	1.00
Pulmonary edema	4 (6.6%)	2 (7.1%)	2 (6.1%)	1.00

AKI=acute kidney injury, CPR=cardiopulmonary resuscitation, MACCE=major adverse cardiac and cerebrovascular events, PCI=percutaneous coronary intervention.

Table 4
Univariate and multivariate analysis.

Predictor variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Age, 10 y	1.79	1.00–3.20	.05	2.40	1.18–4.89	.02
Procedural success	0.24	0.07–0.78	.02	0.17	0.04–0.76	.02
Procedural duration, 10 min	1.30	1.05–1.63	.02	1.28	1.00–1.64	.05
Coronary segments involved	1.18	0.98–1.42	.08	1.10	0.86–1.42	.44
In-hospital AKI, all stages	3.18	0.91–11.08	.07	1.65	0.33–8.20	.54
Impella-support (protected PCI)	1.33	0.44–4.04	.61			
ACS	1.65	0.52–5.23	.39			
Severe CKD	3.80	0.58–25.06	.17			
LogEURO II	1.00	0.91–1.09	.93			
SYNTAX score	1.02	0.98–1.06	.43			
Baseline NYHA-class III or IV	0.67	0.21–2.12	.49			
Baseline CCS III or IV	1.07	0.35–3.25	.91			

ACS=acute coronary syndrome, AKI=acute kidney injury, CI=confidence interval, CKD=chronic kidney disease, MACCE=major adverse cardiac and cerebrovascular events, OR=odds ratio, PCI=percutaneous coronary intervention.

device. Long-term MACCE rates in protected PCI patients in our study were comparable to the results of 2 trials that conducted a 1-year follow-up in which MACCE incidence ranged between 30% and 37%.^[20,23] However, we could not find a difference between protected and unprotected PCI. Procedural success, defined as complete revascularization in the absence of in-hospital major clinical complications was the only variable that was independently associated with improved long-term MACCE in our study, while increased age and duration of intervention were associated with worse outcomes. This finding confirms the results of previous studies and highlights the importance of complete revascularization in MVD in nonemergent patients.^[24] Although not reaching statistical significance, patients undergoing protected PCI reached higher rates of angiographic and procedural success in combination with a lower rate of residual stenosis despite a significantly higher SYNTAX score at baseline. We hypothesize that protected PCI provides improved hemodynamic stability and thus allows for more extensive revascularization. It needs

to be seen whether this finding may be repeated in larger, adequately powered trials and whether it may influence long-term outcome.

A recently published systematic review reported the outcomes of controlled and uncontrolled studies of high-risk PCI with Impella 2.5-support, the majority being 30-day MACCE.^[10] MACCE in the controlled studies ranged between 15% and 35% during a 30-day follow-up whereas uncontrolled studies demonstrated considerably lower 30-day MACCE between 5% and 20%.^[12–14,25–27] Compared to intraaortic balloon pump, protected PCI with the Impella showed a trend toward lower MACCE after 90 days while there was no difference after 30 days.^[13] With an in-hospital MACCE rate of 3.6% in the protected PCI group, our study demonstrated lower short-term outcomes of protected PCI patients compared to prior studies, potentially attributable to the implementation of a structured, dedicated protected PCI program. It has to be noted however that we reported in-hospital MACCE in contrast to 30-day follow-up used by other studies.

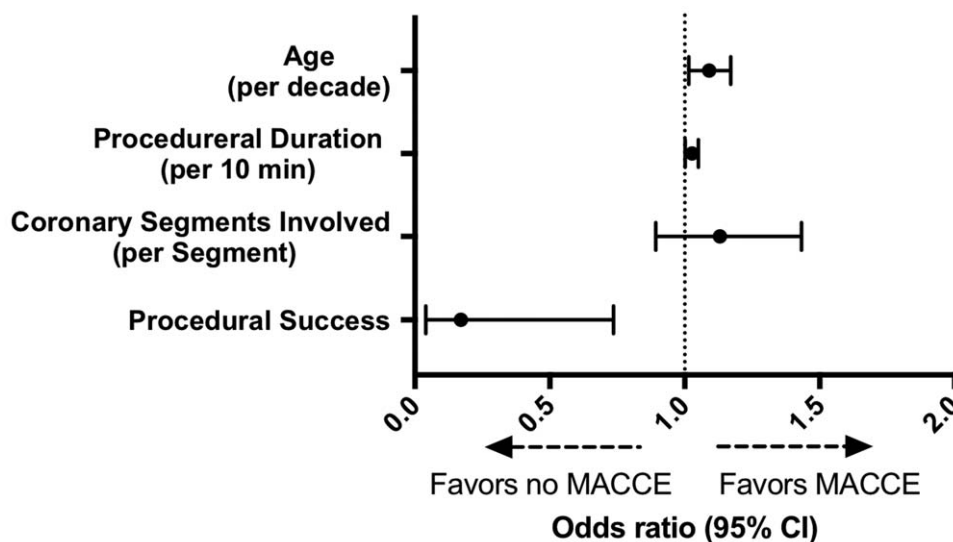


Figure 2. Multivariate regression analysis for predictors of long-term MACCE. CI=confidence interval, MACCE=major adverse cardiac and cerebrovascular event.

Interestingly, a difference can be found in the incidence of AKI in patients undergoing protected PCI when comparing to our prior studies. The PROTECT II trial demonstrated acute renal dysfunction in the Impella group in 4.2% of patients during a 30-day follow-up and further studies reported incidences of acute renal dysfunction between 2% and 5%.^[12–14,28] These rates are significantly lower compared to our reported findings with an incidence of AKI of 24.6%. Additionally, we found no differences comparing protected versus unprotected PCI. These findings are not consistent with the results of recently published retrospective, single-centre study by Flaherty et al demonstrating a beneficial effect of protected PCI with the Impella 2.5 on AKI. This study reported a renal protective effect of the Impella 2.5 in 115 patients undergoing high-risk PCI with severely reduced LVEF compared to 115 matched controls.^[15] The risk of developing AKI was significantly reduced in the Impella group and postprocedural AKI as well as the need for hemodialysis was significantly increased in patients undergoing unprotected PCI without Impella 2.5 support. Of note, severe CKD (defined as glomerular filtration rate $<30\text{ mL/min/1.73}^2$) was significantly more frequent in unprotected PCI patients and patients with severe CKD at baseline had the highest incidence of AKI and hemodialysis regardless of revascularization strategy.

These differing results may be explained by heterogeneous definitions of renal endpoints between the studies and a generally higher prevalence of severe CKD at baseline in the Impella group in our study. The PROTECT II trial defined acute renal dysfunction as the need for dialysis in patients that did not previously require dialysis as well as AKIN II and AKIN III kidney injury. Using the PROTECT II renal endpoints, only 8.2% of our patients suffered post-interventional acute renal dysfunction, which is comparable to the 4.5% in the PROTECT II study given the higher rate of baseline CKD in our study. Compared to Flaherty et al, the prevalence of severe CKD was significantly higher in the Impella group in our study while severe CKD was more prevalent in the unprotected group in their study. Patients with severe CKD undergoing protected PCI had the highest risk of developing AKI in the Flaherty study compared to patients with mild to moderate CKD. The differences in severe CKD between protected and unprotected PCI at baseline may hence account for the missing protective effect of protected PCI in our study. The overall rate of AKI after high-risk PCI comparing the 2 studies is however comparable (24.6% in the present study vs 17.0% reported by Flaherty et al) as well as the mean volume of contrast media used during the interventions ($229 \pm 87\text{ mL}$ in the present study vs $273 \pm 83\text{ mL}$ reported by Flaherty et al).

In conclusion, our study demonstrates a similar long-term and short-term outcome in patients undergoing protected compared to unprotected PCI for MVD in the setting of severely reduced LVEF. Although the beneficial hemodynamic impact of Impella support has been shown in a number of studies,^[13,29,30] this effect did not translate into an improved clinical short- or long-term outcome. Similar to employing the Impella in the setting of cardiogenic shock, careful patient selection may improve the outcome of protected PCI. Future studies should aim to define criteria to identify patients that may benefit from protected PCI.

5. Limitations

The design of our study introduces a number of limitations. First, the number of patients enrolled may restrict the power of the study to detect differences in short- and long-term MACCE. It remains to be seen whether trends and findings demonstrated in

our study are repeatable in larger studies or registries. Second, we combined inclusion periods before and after the implementation of our dedicated protected PCI program, potentially introducing a selection bias. Lastly, significantly more males were in the protected compared to the unprotected PCI group. As gender may influence treatment and outcome in cardiovascular disease, this may limit the generalizability of our results.

6. Conclusions

Patients with MVD and severely depressed LVEF undergoing protected PCI with the Impella 2.5 demonstrate similar in-hospital and long-term outcomes in terms of MACCE and post-procedural adverse events compared to unprotected PCI.

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