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Outcomes of bailout percutaneous ventricular assist device versus prophylactic strategy in patients undergoing nonemergent percutaneous coronary intervention

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Abstract

Objectives: To compare in-hospital outcomes of bailout support to prophylactic support with percutaneous ventricular assist devices (pVAD) for high-risk nonemergent percutaneous coronary intervention (HRPCI).

Background: Prophylactic support with pVAD for a HRPCI is used in patients felt to be at risk for hemodynamic collapse during PCI. An alternative strategy of bailout pVAD support in the event of hemodynamic collapse is also entertained.

Methods: We compared the outcomes of patients entered in the cVAD database who underwent Impella Protected PCI (ProPCI group) with patients from the cVAD and USpella databases receiving bailout Impella support for hemodynamic collapse during HRPCI (Bailout group).

Results: A total of 1,028 patients supported with Impella pVAD were entered into the cVAD database as of July 2019 and were included in this analysis. Of those 971 were in the ProPCI group and 57 in the Bailout group. Patients in the Bailout group were more often female (50.9%vs. 27.2%, p = .0002) with higher median baseline left ventricular ejection fraction (LVEF) (40%vs. 30%, p < .0001) and with lower

Abbreviations: CS, cardiogenic shock; cVAD Study, catheter based ventricular assist device study; HRPCI, high-risk PCI; LVEF, left ventricular ejection fraction; ProPCI, protected PCI; PSM, propensity score match.

prevalence of both heart failure (42.1%vs. 56.9%, p = .0385) and left main disease (40.0%vs. 56.1%, p = .0250) compared to the ProPCI group. Unadjusted and adjusted in-hospital mortality was significantly higher in the Bailout group (49.1%vs. 4.3%, and 57.8%vs. 4.4%, p < .0001 for both).

Conclusions: In our study population, the bailout group was associated with significant increased mortality compared to ProPCI group. Female gender was more frequently observed in patients requiring bailout pVAD. Further investigation is warranted in order to generalize the findings of our study.

KEYWORDS

complex PCI, coronary artery disease, ECMO/IABP/Tandem/Impella, mechanical circulatory support, percutaneous coronary intervention

1 | INTRODUCTION

Long-term benefits of percutaneous coronary intervention (PCI) depend on the ability to achieve optimal procedural results and complete revascularization. Prophylactic hemodynamic support with the percutaneous ventricular assist device (pVAD) Impella (Abiomed, Danvers, MA) in hemodynamically stable patients undergoing high-risk percutaneous coronary intervention (HRPCI) is a strategy to achieve the long-term clinical benefits of PCI.[1,2] This strategy of Impella support to protect hemodynamic stability during complex or lengthy PCI procedures has been forwarded for over a decade and was the hypothesis of the PROTECT II randomized controlled trial (RCT) comparing Impella and IABP support in an HRPCI patient population.[3] Ultimately, performance on the primary endpoint of 30-day composite major adverse event (MAE) rate did not demonstrate significant superiority of Impella, and the trial was ended early. However, analysis of the secondary endpoint of 90-day MAE rate found improved clinical outcome in the Impella arm by this timepoint, attaining significance in those treated per the protocol. To date, evidence affirming protective Impella support for HRPCI has largely been limited to observational and registry studies, though this hypothesis will be more rigorously assessed in the upcoming PROTECT IV RCT, which will reflect a decade of evolving best practices regarding both HRPCI strategy, and HRPCI patient identification, as well.

Patients at high risk for intraprocedural complications comprise a spectrum of patients with anatomically complex coronary disease, significant comorbidities or severely depressed left ventricular ejection fraction (LVEF). This group of patients is frequently comprised of surgical turndowns, with PCI being the only coronary revascularization option.[3]

In some patients perceived as being at lower risk for hemodynamic collapse during PCI, physicians may prefer a bailout hemodynamic support strategy over a planned prophylactic strategy. Clinical outcomes for patients who develop hemodynamic collapse leading to cardiogenic shock (CS) during a nonemergent HRPCI[4] and requiring emergent pVAD initiation as a bailout strategy are not well studied. The objectives of this study were to assess the outcomes of patients receiving pVAD Impella as a bailout strategy for hemodynamic collapse during a nonemergent PCI and to identify characteristics distinguishing this population from those prospectively determined to be HRPCI and treated with prophylactic pVAD Impella support.

2 | METHODS

2.1 | Study design and data collection

As of September 2019, the global cVAD registry has enrolled 4,256 patients treated with Impella devices at 65 sites in the United States. Details on the cVAD registry design have been published previously.[4] Briefly,[5] the initial Impella registry (USpella) was an investigator-initiated retrospective registry that started collecting data in 2009 on all patients supported with Impella pVADs regardless of the indication for support. In December 2016, a total of 2,874 patients had been enrolled at 59 centers. In January 2017, the USpella registry[45] was transitioned to the Global cVAD (catheter based Ventricular Assist Device) registry[45], a prospective, observational, multicenter study collecting data on patients receiving Impella pVADs in daily routine clinical care per institutional standards at physician's discretion. The cVAD prospective study was also designed in collaboration with the Food and Drug Administration (FDA) to collect data on five post approval studies to fulfill the premarket approval application (PMA) regulatory requirements. These post approval studies include the PROTECT III prospective study mandated by the FDA and designed to collect data on patients supported prophylactically with Impella 2.5 or CP during a nonemergent HRPCI. The patients included in the PROTECT III study represent the most contemporary Protected PCI cohort treated by expert PCI operators and Impella users who are proficient at identifying patients likely to benefit from prophylactic support for a nonemergent HRPCI. For these reasons the PROTECT III prospective cohort serves as the control group in this study. The cVAD study received proper ethical oversight at each participating institution through local Institutional Review Boards (IRB)/Ethical Committees (EC) or Western Institutional Review Board.

2.2 | Patient selection

Inclusion criteria for the Bailout group included patients undergoing nonemergent PCI requiring bailout pVAD Impella support during the PCI procedure due to hemodynamic collapse or cardiogenic shock. Unstable patients such as those with cardiac arrest prior to hospital admission or in cardiogenic shock (or not hemodynamically stable) on presentation to the cath lab were excluded. Patients admitted with ST elevation myocardial infraction (STEMI) who underwent emergent PCI were also excluded from the analysis. A total of 57 consecutive subjects in the Bailout group were included in this analysis. Of these, 40 were entered from the global cVAD registry and 17 from the USpella registry. A flow chart illustrating the bailout patient selection process is displayed in Figure 1. Patients receiving bailout Impella support underwent study source document review to characterize the intraprocedural complication leading to hemodynamic collapse.

Of the 4,256 patients enrolled in the cVAD registry through September 1, 2019,541 hemodynamically stable patients received pVAD Impella support prophylactically prior to a nonemergent PCI. Among these, 971 were enrolled in the prospective PROTECT III study and comprised the ProPCI group for this analysis.

2.3 | Device description

The Impella registries comprise patients treated with the full range of Impella Left Ventricular Assist Devices (Impella 2.5®, Impella CP®, Impella 5.0 ®, and Impella LD®). The Impella 2.5 and Impella CP pVADs both received FDA approval for the expanded indication of providing temporary (<6 h) hemodynamic support for elective or urgent PCI in February 2018. Details on their respective device designs and the hemodynamic principles underpinning their mechanism of action have been published previously.[6] Briefly, the Impella CP and 2.5 heart pumps are positioned in the left ventricle via 9 Fr catheters, are powered by 14 Fr and 12 Fr pump motors, respectively, and enable hemodynamic flow of 4.3 L/m and 2.5 L/m, respectively.

2.4 | Definitions

To allow for consistency and for study results comparability, adverse event definitions in the USpella registry and the cVAD study have been consistent with those used in the PROTECT II randomized controlled trial. Major adverse cardiac and cerebrovascular event (MACCE) rate inclusive of death, MI, stroke/TIA, and revascularization were collected in this study.[3-5] Acute renal dysfunction, hypotension during support and cardiopulmonary resuscitation (CPR) or ventricular arrhythmia and acute kidney injury (AKI) were also collected.[5]

2.5 | Statistical analysis

A September 17, 2019 cVAD data export provided the data for the present analysis. Baseline demographic, hemodynamic, clinicopathologic, procedural, and anatomic characteristics were compared across the Bailout and ProPCI groups with outcomes through hospital discharge. In the Bailout group, separate subgroup analyses were conducted and stratified by gender, intraprocedural complication type triggering hemodynamic collapse (coronary dissection/perforation versus refractory hypotensive event), and survival status at time of hospital discharge. Between group differences were analyzed using a Mann–Whitney *U*-test for continuous variables and a Fisher's exact test for categorical variables. Cohort and subgroup comparisons were performed with unpaired t tests and chi square tests. Continuous data

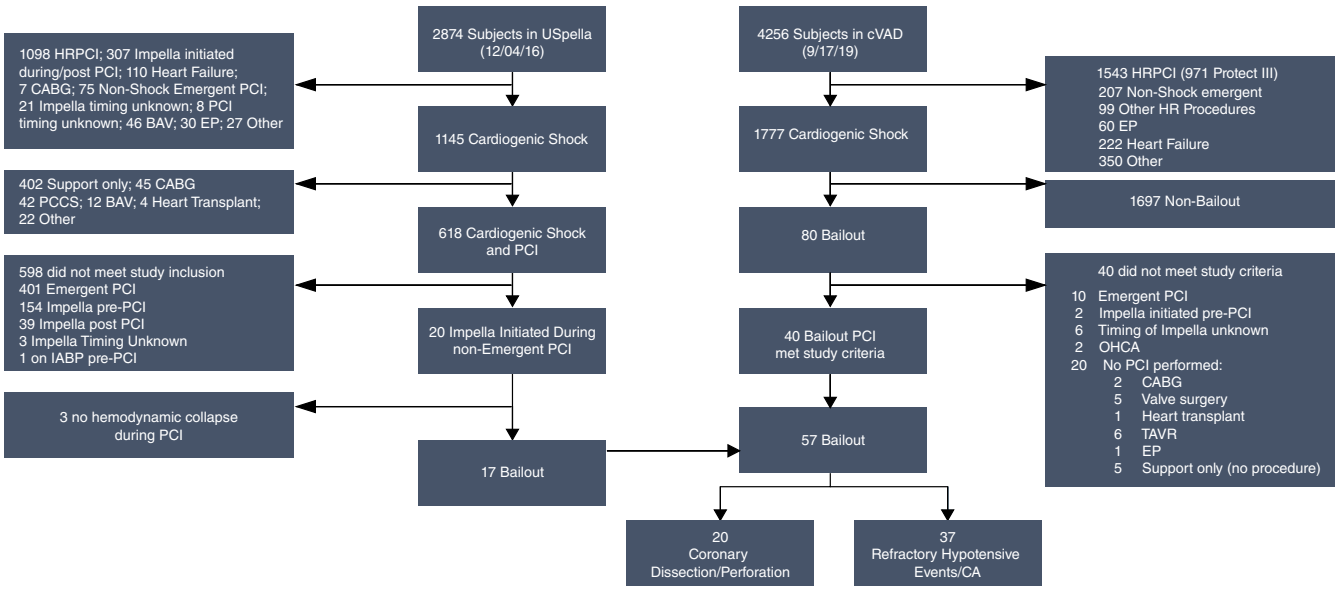

FIGURE 1 Flow diagram of Bailout subject selection [Color figure can be viewed at wileyonlinelibrary.com]

are presented as median (first and third quartile) and categorical data are presented as percentage (numerator / denominator). A p value <0.05 was considered significant. Variables identified as significant in the overall cohort or subgroup analysis were inputted into a multivariate logistic regression model. To identify independent predictors of a bailout strategy we performed a logistic regression with 918 patients (46 in the Bailout group and 872 in the ProPCI group) using age, gender, body surface area (BSA), history of PCI, LVEF, timing of PCI (elective/urgent), heart rate, and distal lesion treated. To identify independent predictors of in-hospital mortality in the entire study population we performed a logistic regression with 918 patients (60 expired during hospital stay and 858 survived to discharge) using age, gender, BSA, history of PCI, LVEF, timing of PCI (elective/urgent), timing of Impella initiation (during PCI/pre PCI), heart rate, and distal lesion treated. We also used these same variables with the exception of timing of Impella initiation to perform logistic regressions to identify independent predictors of in-hospital mortality in the Bailout group with 46 patients (23 expired during hospital stay and 23 survived to discharge) and in the ProPCI group with 835 patients (37 expired during hospital stay and 835 survived to discharge). Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

2.6 | Propensity score matching

A secondary aim of our analysis was to conduct a propensity-matched comparison of outcomes in patients undergoing Impella-protected PCI versus patients receiving bailout Impella support, to adjust for differences between the two groups and determine how distinct indications for Impella placement impact mortality and other clinical outcomes in populations with otherwise similar demographic and baseline characteristics. Propensity scores were generated using 24 admissions, demographic, hemodynamic, anatomic and procedural characteristics. Propensity scores for Bailout and ProPCI patients were matched with 45 pairs. Propensity matching was performed based on optimal matching of one control unit to each unit in the treated group in order to minimize the total within-pair difference. The caliper width was set at 0.25, ensuring that the logits of the propensity scores for pairs of individuals from the two groups should be less than or equal to 0.25 times the pooled estimate of the common standard deviation of the logits of the propensity score. The covariate balance after matching was assessed by the standardized mean difference. A covariate was considered well balanced if the standardized mean difference was <0.25.

3 | RESULTS

3.1 | Baseline characteristics

A higher proportion of the Bailout group was comprised of females compared to the ProPCI group (50.9% vs. 27.2%; p = .0002); the bailout group also presented with a lower prevalence of hypertension (73.7% vs. 90.6%, p = .0003) and heart failure (42.1% vs. 56.9%, p = .0385), respectively (Table 1). Left ventricular ejection fraction (LVEF) was significantly higher in the bailout group (40% vs. 30%, p < .0001), as was baseline heart rate (89.5 vs. 75 bpm; p < .0001).

3.2 | Admission and procedural characteristics

Bailout patients were less likely to be treated for left main disease (40.0% vs. 56.1%; p = .025) or stable angina (22.2% vs. 43.9%; p = .002), but more likely to present with STEMI or NSTEMI (Table 2). Patients in both the Bailout and ProPCI groups were predominantly treated with the Impella CP device (71.4% and 64.6%, respectively), with all remaining patients treated with the Impella 2.5 (excepting 1 bailout patient treated with Impella 5.0). Duration of pVAD Impella support was significantly longer in the Bailout group (20.8 h vs. 1.5 h; p < .0001; Table 3) whereas use of atherectomy was less frequent (29.8% vs. 54.0%, p = .0014). The number of vessels and lesions treated were significantly lower than in the ProPCI group (p = .022 and p = .016, respectively; Table 4). Baseline and post TIMI flows were both significantly lower in the Bailout group (Table 4). Post-PCI TIMI flow 3 was significantly lower in the Bailout group (83.7% vs. 94.6%, p = .002).

In the Bailout group, a refractory hypotensive event was the intraprocedural procedural complication leading to hemodynamic collapse in 37 patients and a coronary dissection or coronary perforation in 20 patients.

Patient status at time of pVAD Impella removal differed significantly between the two groups: under half of Bailout patients (47.9%) were successfully weaned off Impella support following recovery, whereas nearly all ProPCI patients (96.9%) had Impella removal following recovery (*p* < .0001). In the Bailout group, 20.8% of patients had Impella removal due to withdrawal of care (compared to 0.2% of ProPCI patients, p < .0001), and 20.8% of Bailout patients expired while on support (compared to 0.5% of ProPCI patients, p < .0001). After Impella removal, an additional device was implanted in 11.1% of Bailout patients compared to 2.8% of ProPCI patients (p = .006). The intensive care unit length of stay was significantly longer in the Bailout group (4 vs. 3 days; p = .02), whereas the hospital length of stay did not (Table 3).

Cox multivariate logistic regression analysis was performed to determine baseline and anatomic variables predictive of Impella initiation for bailout use during PCI (as opposed to prophylactic Impella support). Female gender was the most significant factor identified (Odds ratio 2.83; 95% CI 1.42–5.66; p = .003), while higher heart rate, higher LVEF, and younger age were also identified as significant factors associated with bailout Impella use (Table 5).

3.3 | Outcomes

The rate of MACCE, and mortality were significantly higher in the Bailout group (p < .0001 for both) (Table 6). Mortality on-support or

TABLE 1 Baseline characteristics in all Bailout and ProPCI patients and in propensity score matched cohorts

	All patients			Propensity score matched cohorts		
	Bailout($N = 57$)	**ProPCI ($N = 971$)**	**p value**	**Bailout($N = 45$)**	**ProPCI ($N = 45$)**	**p value**
Age, (years); median (IQR)	71 (26–95) $N = 57$	72 (35–95) $N = 971$	.36	72 (26–95) $N = 45$	71 (42–90) $N = 45$	.65
Female	50.9% (29/57)	27.2% (264/971)	.0002	48.9% (22/45)	48.9% (22/45)	.99
Race			.048			.57
Black or African American	15.1% (8/53)	13.8% (114/829)		15.6% (7/45)	11.1% (5/45)	
Asian	0% (0/53)	4.3% (36/829)		0% (0/45)	4.4% (2/45)	
AIAN/NHOPI	1.9% (1/53)	0.6% (5/829)		2.2% (1/45)	0% (0/45)	
White	77.4% (41/53)	78.8% (653/829)		75.6% (34/45)	80.0% (36/45)	
Other	5.7% (3/53)	2.5% (21/829)		6.7% (3/45)	4.4% (2/45)	
Body surface area (m^2)	1.9 (1.2–2.4) $N = 57$	1.9 (1.3–2.7) $N = 964$	.049	1.9 (1.3–2.4) $N = 45$	1.8 (1.5–2.2) $N = 45$	.71
LVEF (%), median (IQR)	40% (10–66) $N = 49$	30% (5–72) $N = 618$	< .0001	40% (9.4–66) $N = 45$	35% (10–65%) $N = 45$	.44
Heart rate (bpm), median (IQR)	89.5 (30–153) $N = 50$	75 (19–247) $N = 898$	< .0001	89 (30–153) $N = 39$	76 (38–117) $N = 42$	.0005
Mean arterial BP (mmHg), median (IQR)	84 (34–159) $N = 51$	87 (42–148) $N = 907$	.25	84 (37–144) $N = 40$	81 (59–119) $N = 41$	.93
Medical history						
Prior myocardial infarction	30.9% (17/55)	40.6% (377/929)	.20	30.2% (13/43)	20.0% (9/45)	.33
History of angina	51.9% (28/54)	41.9% (390/930)	.16	51.2% (22/43)	44.4% (20/45)	.67
Heart failure	42.1% (24/57)	56.9% (542/953)	.039	40.0% (18/45)	40.0% (18/45)	.99
NYHA III/IV at admission	50.0% (4/8)	73.0% (278/381)	.22	40.0% (2/5)	73.7% (14/19)	.29
AICD/pacer	8.8% (5/57)	17.0% (164/964)	.14	8.9% (4/45)	6.7% (3/45)	.99
Arrhythmia	24.6% (14/57)	27.1% (257/948)	.76	24.4% (11/45)	15.6% (7/45)	.43
Prior PCI	36.8% (21/57)	39.2% (374/953)	.78	40.0% (18/45)	28.9% (13/45)	.38
Prior CABG	22.8% (13/57)	14.4% (139/962)	.088	15.6% (7/45)	13.3% (6/45)	.99
PVD	10.5% (6/57)	20.2% (192/950)	.086	13.3% (6/45)	11.1% (5/45)	.99
Prior stroke/TIA	7.0% (4/57)	16.0% (153/956)	.088	6.7% (3/45)	2.2% (1/45)	.62
Diabetes	46.4% (26/56)	54.5% (524/962)	.2707	48.9% (22/45)	44.4% (20/45)	.83
Hypertension	73.7% (42/57)	90.6% (871/961)	.0003	77.8% (35/45)	75.6% (34/45)	.99
COPD	32.1% (18/56)	21.7% (206/951)	.071	35.6% (16/45)	28.9% (13/45)	.65

(Continues)

TABLE 1 (Continued)

	All patients			Propensity score matched cohorts		
	Bailout($N = 57$)	ProPCI ($N = 971$)	p value	Bailout($N = 45$)	ProPCI ($N = 45$)	p value
Renal insufficiency	19.3% (11/57)	26.1% (249/954)	.28	24.4% (11/45)	22.2% (10/45)	.99
Smoking	49.1% (27/55)	61.1% (576/942)	.088	48.9% (22/45)	46.7% (21/45)	.99

Abbreviations: AIAN/NHOPI, American Indian, Alaska Native / Native Hawaiian, Other Pacific Islander; AICD, automated implantable cardioverter defibrillator; BP, blood pressure, CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disorder; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack.

following withdrawal of care was 41.7% and 0.7% in the Bailout and ProPCI groups, respectively. In-hospital mortality rates were 49.1% and 4.3% in the Bailout and ProPCI groups, respectively ($p < .0001$, Figure 2).

Cox multivariate logistic regression was performed to assess predictive factors of in-hospital mortality across all patients. Age (OR 1.06 for each year; 95% CI 1.03–1.10, $p < .0001$) and higher heart rate (OR 1.02 for each beat per minute; 95% CI 1.01–1.03, $p = .003$) were both predictive factors, as was the use of bailout Impella (OR 23.23; 95% CI 10.45–51.78; $p < .0001$) (Table 7).

3.4 | Bailout subgroup analyses

Bailout subgroup analyses were performed to compare characteristics and outcomes stratified by gender, by intraprocedural complication type (coronary dissection/perforation vs. refractory hypotensive events), and by survival status through hospital discharge (Supplemental Tables S3–S8). Patients who experienced refractory hypotensive events leading to hemodynamic collapse during PCI had significantly lower mean arterial blood pressure at baseline assessment compared to those with coronary dissection or perforation (74.7 mmHg vs. 99.0 mmHg; $p = .0140$) and were twice as likely to smoke (60% vs. 30%; $p = .0496$).

Bailout patients who died prior to hospital discharge were significantly older than patients surviving through discharge (78 vs. 62 years; $p = 0.0005$). Most patients who died prior to discharge had a prior PCI procedure (53.6% vs. 20.7%; $p = .0140$). These patients were treated with a significantly higher number of inotropes during Impella placement (median 3 vs. 2; $p = .031$), with the extent of inotropic support constituting the most significant procedural difference between the patients who died versus those who survived through discharge. Patients who died prior to discharge were more likely to have a distal lesion treated (46.4% vs. 20.0%; $p = .08$); a distal lesion treated was also more prevalent in patients experiencing a coronary dissection (55.6% vs. 22.9%; $p = .03$).

Regression analysis performed exclusively in the Bailout group found solely age to be a significant predictor of in-hospital mortality (OR 1.08 per year; 95% CI 1.01–1.15, $p = .016$) (Table S1). However, in the ProPCI group, age (OR 1.05 per year; 95% CI 1.01–1.09, $p = .007$) and heart rate (OR 1.02 per beat per minute; 95% CI 1.01–1.04, $p = .007$) were significant predictors of in-hospital mortality (Table S2).

3.5 | Propensity score matched cohort comparison

Propensity score matched cohorts of 45 Bailout patients and 45 ProPCI patients were created on the basis of 24 covariates. This comparison of characteristics and outcomes is presented in the right-hand columns of Tables 1-5. Mortality rates in the propensity-matched Bailout group was significantly higher than in the ProPCI group (57.8% vs. 4.4%; $p < .0001$).

TABLE 2 Hospital admission characteristics

	All patients			Propensity score matched cohorts		
	Bailout($N = 57$)	ProPCI ($N = 971$)	p value	Bailout($N = 45$)	ProPCI($N = 45$)	p value
Transferred from another hospital	41.3% (19/46)	50.4% (336/667)	.29	40.0% (14/35)	55.6% (15/27)	.31
Diagnosis at admission			.002			.49
Angina	22.2% (8/36)	43.9% (237/540)		19.4% (6/31)	34.6% (9/26)	
NSTEMI	58.3% (21/36)	50.2% (271/540)		58.1% (18/31)	50.0% (13/26)	
STEMI	19.4% (7/36)	5.9% (32/540)		22.6% (7/31)	15.4% (4/26)	
Left main disease	40.0% (22/55)	56.1% (539/960)	.03	42.2% (19/45)	40.0% (18/45)	.99
Last remaining conduit	17.0% (9/53)	13.2% (115/873)	.41	18.6% (8/43)	9.5% (4/42)	.35
CABG denied	51.9% (27/52)	52.6% (457/869)	.99	52.4% (22/42)	62.8% (27/43)	.38
PCI status						
Elective	43.9% (25/57)	53.6% (520/971)	.17	37.8% (17/45)	28.9% (13/45)	.50
Urgent	56.1% (32/57)	46.4% (451/971)	.17	62.2% (28/45)	71.1% (32/45)	.50

Abbreviations: CABG, coronary artery bypass graft; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction.

4 | DISCUSSION

This study provides insight into the clinical outcomes for the use of provisional bailout pVAD Impella support during high-risk PCI and defines the associated patient characteristics. The primary findings are: (1) A bailout strategy for hemodynamic collapse in patients undergoing a nonemergent PCI is associated with very high mortality; (2) Female gender, higher heart rate, higher LVEF, and younger age as four significant distinguishing characteristics among patients receiving bailout Impella pVAD support, following onset of hemodynamic collapse during a nonemergent PCI; (3) For the entire study cohort, advanced age and higher heart rate were determined to be independent predictors of in-hospital mortality while prophylactic use of the pVAD Impella in nonemergent PCI was found to be an independent predictor of survival; (4) In the Bailout group, age was found to be an independent predictor of mortality whereas in the ProPCI group in addition to age, elevated heart rate was an independent predictors of in-hospital mortality.

In our study patient population, we observed that patients prospectively identified as requiring prophylactic support resembled the conventional high risk PCI patient profile with significant patients undergoing unprotected left main PCI, with lower ejection fraction and having a history of congestive heart failure as compared to the bailout patients.

The use of bailout Impella support following development of intraprocedural hemodynamic compromise emerged as the most significant factor for mortality, with a 23.23 times higher risk for in-hospital mortality. This suggests that hemodynamic collapse prompting mechanical circulatory support, however timely, is associated with similar mortality as historically observed in cardiogenic shock.

Other notable findings from this analysis include a significant variance in atherectomy rates across the two groups, with ProPCI patients undergoing atherectomy at a higher rate prior to stenting. The number of treated vessels was also much higher in the ProPCI group suggesting that the development of CS necessitated a shift in focus from pursuing complete revascularization to ensuring patient survival.

In this analysis, four baseline characteristics were associated with the need for bailout pVAD Impella support following hemodynamic collapse during PCI - female gender, higher LVEF, higher heart rate, and younger age. In our analysis, women were 2.8 times more likely to require bailout MCS support. The finding that women were frequently not identified as HRPCI and necessitating prophylactic pVAD Impella support is not surprising. A study of 133 consecutive patients with depressed LVEF undergoing elective PCI at a single Italian center from 1998–2000 also compared early outcomes among those patients receiving prophylactic IABP support (Group A) and those undergoing PCI with provisional IABP support (Group B).[7] Briguori et al reported that 15% of Group B ultimately experienced severe hypotension and/or shock and required urgent IABP support, whereas hemodynamic stability was preserved in all Group A patients.[8] The authors identified female gender and jeopardy score as significant predictors of hypotension/shock, with females at 2.7× higher risk for adverse events. Elective use of IABP was found to be protective for hypotension/shock, at 0.11× risk. The authors concluded that elective IABP support for HRPCI is associated with favorable outcomes compared to provisional support, particularly in females.[7]

In our study, women were more likely to have a history of angina, renal insufficiency, and peripheral vascular disease – as has been observed across numerous gender analyses within interventional cardiology studies.[9] Men were more likely to have depressed LVEF, prior history of MI, and prior CABG. The preserved LV function observed in women particularly women who ultimately required bailout Impella support– is likely the most significant indicator for why these patients

TABLE 3 Procedural characteristics

	All patients			Propensity score matched cohorts		
	Bailout($N = 57$)	ProPCI ($N = 971$)	p value	Bailout($N = 45$)	ProPCI($N = 45$)	p value
Impella device			.022			.20
Impella 2.5	26.8% (15/56)	35.3% (343/971)		31.8% (14/44)	46.7% (21/45)	
Impella CP	71.4% (40/56)	64.7% (628/971)		2.3% (1/44)	0%	
Impella 5.0	1.8% (1/56)	0%		65.9% (29/44)	53.3% (24/45)	
Impella access			.71			.71
Femoral	100.0% (40/40)	94.1% (913/970)		100.0% (30/30)	93.3% (42/45)	
Subclavian	0% (0/40)	0.8% (8/970)		0% (0/30)	4.4% (2/45)	
Other	0% (0/40)	5.1% (49/970)		0% (0/30)	2.2% (1/45)	
Atherectomy / Rotablation	29.8% (14/47)	54.0% (323/598)	.001	26.3% (10/38)	25.0% (6/24)	.99
Inotropes/vasopressors during Impella support	77.2% (44/57)	12.4% (120/971)	<.0001	82.2% (37/45)	20.0% (9/45)	<.0001
Maximum. No. of different inotropes, median (IQR)	3 (1–6) $N = 44$	1 (1–5) $N = 120$	<.0001	3 (1–6) $N = 37$	1 (1–3) $N = 9$	.0022
Duration of PCI (h), median (IQR)	2.2 (0.5–34.2) $N = 46$	1.9 (0.1–8.3) $N = 892$	.04	2.0 (0.5–34.2) $N = 39$	1.9 (0.6–4.3) $N = 43$	.51
Duration of Impella support (h), median (IQR)	20.8 (0.4–79) $N = 42$	1.5 (0–746) $N = 828$	<.0001	19.0 (0.4–79.0) $N = 35$	1.8 (0.2–196.9) $N = 41$	<.0001
Patient status at time of explant / reason for device explant			<.0001			< .0001
Recovered and mechanical support no longer needed	47.9% (23/48)	96.9% (932/962)		43.6% (17/39)	95.6% (43/45)	
Recovered but experienced DR-AE	2.1% (1/48)	1.7% (16/962)		2.6% (1/39)	2.2% (1/45)	
Did not recover and experienced DR-AE	2.1% (1/48)	0.3% (3/962)		2.6% (1/39)	0% (0/45)	
Expired on support	20.8% (10/48)	0.5% (5/962)		25.6% (10/39)	2.2% (1/45)	
Withdrawal of care and device was turned off / removed	20.8% (10/48)	0.2% (2/962)		20.5% (8/39)	0% (0/45)	
Required device replacement before pump end of life	0% (0/48)	0.3% (3/962)		0% (0/39)	0% (0/45)	
Required a higher level of support	6.3% (3/48)	0.1% (1/962)		5.1% (2/39)	0% (0/45)	
Expired on support or following withdrawal of care	41.7% (20/48)	0.7% (7/962)	<.0001	46.2% (18/39)	2.2% (1/45)	<.0001
ICU stay (days), median (IQR)	4 (0.1–23) $N = 46$	3 (0–41) $N = 473$	.02	4 (0.1–20) $N = 38$	3 (0–21) $N = 26$	.69
Duration of index hospitalization (days), median (IQR)	5.9 (0.6–80.1) $N = 50$	5.9 (0–137.3) $N = 952$	.22	5.3 (0.6–43) $N = 41$	6 (1.1–44.1) $N = 44$	.82

Abbreviations: DR-AE, device-related adverse event; ICU, intensive care unit; PCI, percutaneous coronary intervention.

were not identified as HRPCI. The "triad" of characteristics signaling HRPCI across most proposed definitions can loosely be termed as severe and/or complex coronary disease, significant comorbidity burden, and depressed LV function. Women, however, frequently have an atypical clinical presentation and may present with a preserved LV function.[9,10] Despite preserved LVEF, women often have smaller chamber sizes, stroke volume and the inability to augment cardiac output, thus perhaps are more prone to hemodynamic collapse with ischemia.[10-12] The results of this analysis indicate that the threshold indicating ventricular dysfunction and HRPCI in women should perhaps be higher, and merits exploration in future studies.

Among other factors identified as associated with receiving bailout Impella support was a higher heart rate at baseline (89.5 vs. 75 bpm, respectively). To our knowledge, increases in heart rate within normal range have not been previously included as one of the baseline characteristics signifying HRPCI; however, we would suggest

TABLE 4 Treated lesion characteristics

	All patients			Propensity score matched cohorts		
	Bailout($N = 57$)	ProPCI ($N = 971$)	p value	Bailout($N = 45$)	ProPCI($N = 45$)	p value
No. vessels treated			.022			.25
1	42.1% (16/38)	29.5% (284/964)		41.4% (12/29)	26.7% (12/45)	
2	47.4% (18/38)	41.3% (398/964)		44.8% (13/29)	44.4% (20/45)	
3	10.5% (4/38)	29.3% (282/964)		13.8% (4/29)	28.9% (13/45)	
Vessel location						
Graft	5.4% (3/56)	4.3% (42/967)	.73	0% (0/45)	2.2% (1/45)	.31
LAD	62.5% (35/56)	73.6% (712/967)	.09	66.7% (30/45)	71.1% (32/45)	.82
LCX	51.8% (29/56)	56.4% (545/967)	.58	48.9% (22/45)	62.2% (28/45)	.29
LM	25.0% (14/56)	45.4% (439/967)	.003	28.9% (13/45)	40.0% (18/45)	.38
RCA	37.5% (21/56)	30.8% (298/967)	.30	40.0% (18/45)	28.9% (13/45)	.38
No. lesions treated, median (Q1-Q3)	2 (1–4) $N = 37$	2 (1–10) $N = 968$	.016	2 (1–4) $N = 28$	2 (1–6) $N = 45$	.16
Lesion location						
Distal	34.0% (18/53)	40.3% (382/948)	.39	35.6% (16/45)	40.0% (18/45)	.83
Mid	62.3% (33/53)	56.4% (535/948)	.48	66.7% (30/45)	57.8% (26/45)	.51
Ostial	5.7% (3/53)	19.0% (180/948)	.010	6.7% (3/45)	20.0% (9/45)	.12
Proximal	81.1% (43/53)	73.2% (694/948)	.26	80.0% (36/45)	71.1% (32/45)	.46
Pre TIMI flow			.013			.18
0	23.1% (12/52)	12.7% (111/875)		23.3% (10/43)	12.8% (5/39)	
1	11.5% (6/52)	5.7% (50/875)		11.6% (5/43)	2.6% (1/39)	
2	19.2% (10/52)	15.5% (136/875)		16.3% (7/43)	15.4% (6/39)	
3	46.2% (24/52)	66.1% (578/875)		48.8% (21/43)	69.2% (27/39)	
Post TIMI flow			.004			.52
0	6.1% (3/49)	2.6% (21/817)		7.3% (3/41)	2.7% (1/37)	
1	6.1% (3/49)	0.5% (4/817)		4.9% (2/41)	0% (0/37)	
2	4.1% (2/49)	2.2% (18/817)		4.9% (2/41)	2.7% (1/37)	
3	83.7% (41/49)	94.6% (773/817)		82.9% (34/41)	94.6% (35/37)	

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

that it be considered for future ProPCI risk profiles. A recent meta-analysis of association between heart rate and mortality across 11 studies comprising 156, 374 ACS patients found that higher heart rate at admission (6 studies, 147, 951 patients) was associated with significantly higher rates of in-hospital and long-term mortality (2.04 and 1.63 RR, respectively), with thresholds indicating elevated heart rate defined as >70, ≥ 80, ≥ 82, >90, ≥ 92, or > 130 bpm, per individual study.[11] In our study, higher heart rate was associated with bailout Impella use and in-hospital mortality. In a subset analysis of the Framingham Heart Study, Tofler et al observed that higher heart rate in the setting of ACS may be associated with a prothrombotic state, which itself is associated with endothelial dysfunction.[13] Higher levels of biomarkers indicating endothelial damage at hospital admission have been identified as having a significant correlative relationship with early mortality following CS.[14,15]

Though in-hospital mortality occurred at a higher rate in women (1.76 times elevated risk), gender was not significantly predictive of mortality. Other factors identified as significantly predictive for in-hospital mortality were age and the MCS strategy (bailout as opposed to prophylactic pVAD Impella use during PCI). Advanced aged is not a surprising correlate of mortality. Although an age-based analysis of the PROTECT II[3] patient population found that treatment with Impella in patients aged ≥80 resulted in comparable outcomes to younger patients,[8,16] our analysis is based on an unselected, "real-world" population, in which older patients likely presented with more severe comorbidities and advanced coronary disease.

5 | LIMITATIONS

We are limited by observational design of the study and by the disproportionately larger size of the ProPCI group in comparison to the bailout group. The limited number of patients receiving bailout Impella

TABLE 5 Multivariate logistic regression analysis of predictive factors for Bailout Impella during PCI

Variables	Odds ratio (95% CI)	p value
All patients		
Age (per 1 years)	**0.97 (0.95–1.00)**	**.047**
Female gender	**2.83 (1.42–5.66)**	**.0032**
BSA (per 1 m^2)	0.54 (0.13–2.28)	.40
Heart rate (per 1 bpm)	**1.03 (1.02–1.05)**	**<.0001**
LVEF (per 5%)	**1.19 (1.08–1.32)**	**.0006**
Prior PCI	0.85 (0.44–1.65)	.63
Urgent PCI	1.32 (0.71–2.47)	.39
Distal lesion location	0.51 (0.21–1.28)	.15

Note: Bold values represent the results of this regression model show that Female gender, LVEF, heart rate and age are independent predictors of a bailout strategy.
Abbreviations: BSA, body surface area; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

support in the cVAD study required additional bailout patient enrollment from the retrospective USpella registry. The USpella registry includes an earlier cohort of cases while the comparator group derived from PROTECT III reflects current best practice.

The cVAD and USpella registries comprise specifically patients implanted with Impella devices. The number of patients treated at these centers with a strategy for bailout Impella use that ultimately did not require support is therefore unknown, as are their outcomes. Hence, we are unable to include a control group comprised of these patients, though the frequency with which HRPCI patients treated with a bailout strategy necessitate emergent intraprocedural support is a topic of significant clinical interest for future study. Furthermore, we are limited by an inability to precisely delineate the cause of cardiogenic shock in greater detail, given the available data.

Lastly, the outcomes of patients who crashed during PCI in a setting where Impella devices are not available have not been included in this study. For all these reasons our findings are hypothesis generating and could serve to inform on the design of a randomized controlled

TABLE 6 In-hospital outcomes

	All patients			Propensity score matched cohorts		
	Bailout (N = 57)	ProPCI (N = 971)	p value	Bailout (N = 45)	ProPCI(N = 45)	p value
MACCE	56.1% (32/57)	7.4% (72/971)	<.0001	66.7% (30/45)	11.1% (5/45)	<.0001
Death	49.1% (28/57)	4.3% (42/971)	<.0001	57.8% (26/45)	4.4% (2/45)	<.0001
MI	3.5% (2/57)	1.2% (12/971)	.18	4.4% (2/45)	2.2% (1/45)	.99
Stroke/TIA	3.5% (2/57)	0.8% (8/971)	.102	4.4% (2/45)	2.2% (1/45)	.99
Revascularization	5.3% (3/57)	1.4% (14/971)	.06	6.7% (3/45)	2.2% (1/45)	.62
Acute renal dysfunction	12.3% (7/57)	2.9% (28/971)	.002	15.6% (7/45)	4.4% (2/45)	.16
Acute kidney injury	26.3% (15/57)	6.2% (60/971)	<.0001	26.7% (12/45)	15.6% (7/45)	.30
Hypotension during support	17.5% (10/57)	1.6% (16/971)	<.0001	20.0% (9/45)	4.4% (2/45)	.049
CPR or ventricular arrhythmia	22.8% (13/57)	1.5% (15/971)	<.0001	26.7% (12/45)	0% (0/45)	.0002

Abbreviations: CPR, cardiopulmonary resuscitation; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; TIA, transient ischemic attack.

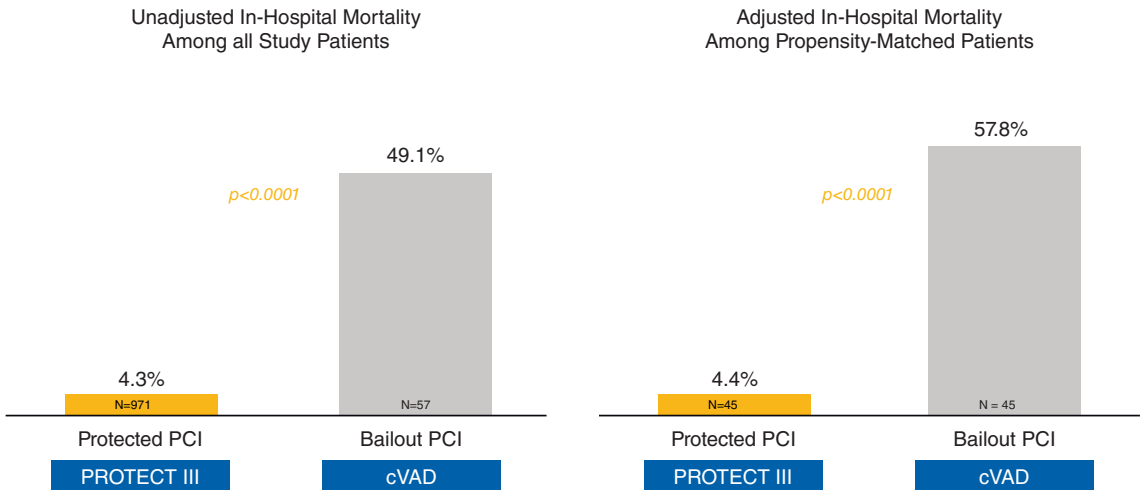

FIGURE 2 In-hospital mortality comparison between Impella Bailout and Impella protected PCI [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 7 Multivariate logistic regression analysis of factors predictive of in-hospital mortality

Variables	Odds ratio (95% CI)	p value
All patients		
Age (per 1 years)	**1.06 (1.03–1.10)**	**<.0001**
Female gender	1.76 (0.89–3.48)	.10
BSA (per 1 m^2)	0.82 (0.19–3.50)	.79
Heart rate (per 1 bpm)	**1.02 (1.01–1.03)**	**.0031**
LVEF (per 5%)	0.95 (0.86–1.05)	.36
Prior PCI	1.18 (0.63–2.21)	.61
Urgent PCI	1.80 (0.97–3.33)	.062
Impella initiated during PCI	**23.23 (10.45–51.78)**	**<.0001**
Distal lesion location	1.42 (0.68–2.93)	.3

Note: Bold values represent the results of this regression model show that Impella initiated during PCI (bailout strategy), age and heart rate are independent predictors of increased in-hospital mortality.
Abbreviations: BSA, body surface area; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

trial comparing elective and bailout strategies which are warranted to generalize our findings.

6 | CONCLUSIONS

In our study population, the bailout group was associated with significant increased mortality compared to ProPCI group. The results of our study suggest that failure to identify patients who may benefit from ProPCI was associated with excessive mortality, despite prompt initiation of pVAD Impella as bailout upon hemodynamic collapse. Women were disproportionately less likely to be identified as high-risk for hemodynamic collapse, perhaps owing to a higher LVEF at presentation compared to men. Subtle increase in heart rate also merits further consideration as a patient characteristic signaling a greater risk for hemodynamic collapse requiring bailout pVAD support during high-risk PCI. Further investigation is warranted in order to generalize the findings of our study.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

Research data are not shared.

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REFERENCES

1. Gossl M, Faxon DP, Bell MR, Holmes DR, Gersh BJ. Complete versus incomplete revascularization with coronary artery bypass graft or percutaneous intervention in stable coronary artery disease. Circ Cardiovasc Interv. 2012;5(4):597-604.
2. Burzotta F, Russo G, Ribichini F, Piccoli A, et al. Long-term outcomes of extent of revascularization in complex high risk and indicated patients undergoing Impella-protected percutaneous coronary intervention: report from the Roma-Verona registry. J Interv Cardiol. 2019;2019:5243913.
3. O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. Circulation. 2012;2(126):1717-1727.
4. Vetrovec GW, Anderson M, Schreiber T, et al. The cVAD registry for percutaneous temporary hemodynamic support: a prospective registry of Impella mechanical circulatory support use in high-risk PCI, cardiogenic shock, and decompensated heart failure. Am Heart J. 2018;199:115-121.
5. Flaherty MP, Moses JW, Westenfeld R, et al. Impella support and acute kidney injury during high-risk percutaneous coronary intervention: the global cVAD renal protection study. Catheter Cardiovasc Interv. 2019;29:672-675.
6. Verma S, Burkhoff D, O'Neill WW. Avoiding hemodynamic collapse during high-risk percutaneous coronary intervention: advanced hemodynamics of impella support. Catheter Cardiovasc Interv. 2017;89(4):672-675.
7. Narins CR, Ling FS, Fischi M, Peterson DR, Bausch J, Zareba W. In-hospital mortality among women undergoing contemporary elective percutaneous coronary intervention: a reexamination of the gender gap. Clin Cardiol. 2006;29(6):254-258.
8. Briguori C, Sarais C, Pagnotta P, et al. Elective versus provisional intra-aortic balloon pumping in high-risk percutaneous transluminal coronary angioplasty. Am Heart J. 2003;145(4):700-707.
9. Duca F, Zotter-Tufaro C, Kammerlander AA, et al. Gender-related differences in heart failure with preserved ejection fraction. Sci Reports. 2018;8(1):1080. https://doi.org/10.1038/s41598-018-19507-7.
10. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, et al. Normal values for cardiovascular magnetic resonance in adults and children. J Cardiovasc Magn Reson. 2015;17:29.

11. Wheatley CM et al. Sex differences in cardiovascular function during submaximal exercise in humans. SpringerPlus. 2014;3:445. https://doi.org/10.1186/2193-1801-3-445.
12. Xu T, Zhan Y, Xiong J, et al. The relationship between heart rate and mortality of patients with acute coronary syndromes in the coronary intervention era: meta-analysis. Medicine (Baltimore). 2016;95(46):e5371.
13. Tofler GH, Massaro J, Levy DA, Sutherland PA, Buckley T, D'Agostino RB. Increased heart rate is associated with a prothrombotic state: the Framingham heart study. Eur J Prev Cardiol. 2017;24(4):382-388.
14. Jung C, Fuernau G, Muench P, et al. Impairment of the endothelial glycocalyx in cardiogenic shock and its prognostic relevance. Shock. 2015;43(5):450-455.
15. Frydland M, Ostrowski SR, Moller JE, et al. Plasma concentration of biomarkers reflecting endothelial cell- and Glycocalyx damage are increased in patients with suspected ST-elevation myocardial infarction complicated by cardiogenic shock. Shock. 2018;50(5):538-544.
16. Pershad A, Fraij G, Massaro JM, et al. Comparison of the use of hemodynamic support in patients >/=80 years versus patients <80 years during high-risk percutaneous coronary interventions (from the multicenter PROTECT II randomized study). Am J Cardiol. 2014;114(5):657-664.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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