Are there etiology-specific risk factors for adverse outcomes in patients on Impella 5.5 support?

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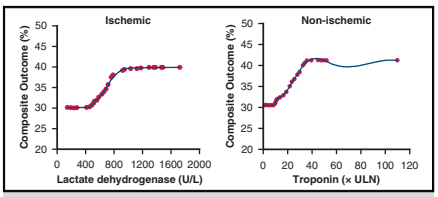
ABSTRACT

Objectives: To identify possible etiology-specific differences in preoperative risk factors for major adverse events during Impella 5.5 support in patients with ischemic (ICM) and nonischemic cardiomyopathy (NICM).

Methods: From October 2019 to January 2023, 228 Impella 5.5 devices were inserted at our institution. Patients were stratified into ICM (n = 124) and NICM (n = 104) cohorts. The primary outcome was a composite of death/stroke/new-onset dialysis while actively receiving Impella 5.5 support. Random forests identified preoperative factors predictive of the primary outcome separately for each cohort, with ranking by variable importance.

Results: The primary outcome occurred in 42 (34%) patients with ICM and 35 (34%) patients with NICM. Twenty-one (17%) patients with ICM and 21 (20%) patients with NICM died on Impella 5.5; stroke occurred in 12 (9.7%) patients with ICM and 3 (2.9%) patients with NICM, and new-onset dialysis was initiated in 23 (19%) patients with ICM and 24 (23%) patients with NICM while actively receiving Impella 5.5 support. Risk factors reflecting systemic and myocardial cellular injury, end-organ and cardiopulmonary failure, right ventricular dysfunction, and smaller left ventricular dimensions were most predictive of adverse outcomes in both cohorts. Indications for Impella 5.5 and device strategy (bridge to recovery, advanced therapies, or decision) were not top risk factors in either cohort.

Conclusions: Risk factors related to preoperative stability, right ventricular dysfunction, and left ventricular size were more predictive of adverse outcomes while actively receiving Impella 5.5 support than indication or device strategy. These factors could help identify high-risk patients who may benefit from additional tailored management to reduce their risk for these impactful adverse outcomes while on Impella 5.5 support. (JTCVS Open 2024;21:123-37)



Top risk factors in ischemic and nonischemic cardiomyopathy cohorts with an Impella 5.5.

CENTRAL MESSAGE

Cellular injury, end-organ and cardiopulmonary failure, RV dysfunction, and small LV size were more predictive of adverse outcomes during Impella 5.5 support than indication or device strategy.

PERSPECTIVE

Assessing markers of cellular injury, end-organ and cardiopulmonary failure, RV dysfunction, and LV size before Impella 5.5 insertion may help refine overall patient selection. These factors were more predictive of a composite outcome of death, stroke, or new-onset dialysis while actively receiving Impella 5.5 support than indication and intended device strategy.

See Discussion on page 138.

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Abbreviations and Acronyms

AMI = acute myocardial infarction
ICM = ischemic cardiomyopathy
Intermacs = Interagency Registry for Mechanically Assisted Circulatory Support
LDH = lactate dehydrogenase
LV = left ventricle
LVAD = left ventricular assist device
LVEDD = left ventricular end-diastolic diameter
NICM = nonischemic cardiomyopathy
PA = pulmonary artery
PAPi = pulmonary artery pulsatility index
RV = right ventricle
tMCS = temporary mechanical circulatory support
VIMP = variable importance

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The Impella 5.5 (Abiomed) is a surgically implanted, temporary microaxial transvalvular left ventricular assist device (LVAD) used across a variety of clinical situations, including in cardiogenic shock and for planned periprocedural hemodynamic support during high-risk cardiac interventions.[1] It is often employed as a component of an overall management program, either as a bridge to recovery, to advanced therapies, or to decision. Although favorable survival among patients supported with Impella 5.5 devices has been reported, adverse outcomes occurring while actively on support can potentially affect the success of these overall programs.[2,3] In addition, because morbidity and mortality vary across etiologies of cardiomyopathy, we hypothesized that differences in risk factors for adverse outcomes while actively receiving Impella 5.5 support may also exist between patients with ischemic cardiomyopathy (ICM) and nonischemic cardiomyopathy (NICM).[2-4] Therefore, to help inform patient selection and optimize management, we aimed to identify both general and etiology-specific risk factors for major adverse outcomes occurring during Impella 5.5 support.

PATIENTS AND METHODS

Patients

From October 2019 to January 2023, 228 consecutive Impella 5.5 devices were implanted in 226 patients at Cleveland Clinic. The unit of analysis was devices (n = 228). One patient with an Impella 5.5 underwent heart transplant and was subsequently supported by another Impella 5.5; this posttransplant device was counted separately (Figure 1). Two patients who underwent Impella 5.5 exchanges were counted twice each, with events for the first device censored at removal. The number of these was sufficiently small that mixed effect statistics were not used. Median age was 63 years (15th/85th percentiles: 44, 73 years) and 43 (19%) patients were female. Devices were inserted via the right axillary artery in 216 (95%), left axillary artery in 8 (3.5%), and direct aortic cannulation in 4 (1.8%) patients. Details of our institutional practices for Impella 5.5 insertion and management are provided in Appendix E1.

Data

Data were collected from medical record review and an institutional quality database. The Cleveland Clinic Institutional Review Board approved this study and publication of these data on January 24, 2023 (#22-022), with informed consent waived.

Indications for Impella 5.5 support were determined by patients' clinical state at insertion and were classified as either cardiogenic shock or assisted high-risk cardiac intervention. Cardiogenic shock was further stratified as either the result of (1) acute myocardial infarction (AMI), (2) decompensated heart failure, (3) postcardiotomy, or (4) other causes. Classification as an assisted high-risk cardiac intervention required that patients undergoing conventional cardiac surgery, ablation for ventricular tachycardia, or percutaneous coronary intervention have Impella 5.5 insertion listed on the preoperative consent form (in contrast to unplanned postcardiotomy insertion).

Intended device strategy, recorded by the surgeon at Impella 5.5 insertion, was either bridge to advanced therapy, bridge to decision, or bridge to recovery. Patients were retrospectively classified into both Interagency Registry for Mechanically Assisted Circulatory Support (Intermacs) profiles 1-7 and Society for Cardiovascular Angiography and Interventions shock stages A-E based on their clinical state at Impella 5.5 insertion.[5,6]

Preoperative echocardiographic and laboratory assessments, invasive pulmonary artery (PA) catheter hemodynamics, inotrope/vasopressor use, and other temporary mechanical circulatory support (tMCS) were recorded from the last available time point before Impella 5.5 insertion. Pulmonary artery pulsatility index (PAPi) was calculated as [PA systolic pressure – PA diastolic pressure]/central venous pressure.

Etiology Cohorts

Each patient's etiology of cardiomyopathy was determined independently from their indication for Impella 5.5 insertion and was defined as either ICM or NICM. The NICM cohort included all patients with idiopathic NICM as well as those with hypertrophic, restrictive, myocarditis, posttransplant primary graft dysfunction/rejection, valvular, or traumatic cardiomyopathy. One patient with mixed ICM/NICM was classified as NICM, as it reflected their predominant clinical phenotype. A total of 124 (56%) Impella 5.5 devices were implanted in patients with ICM and 104 (44%) in patients with NICM (Figure 2). In the ICM and NICM cohorts, median age was 65 years (57, 75) versus 56 years (36, 70), and 22 (18%) versus 21 (20%) were female.

End Points

The primary outcome was a composite of death, stroke, or new-onset dialysis while actively receiving Impella 5.5 support. Death was only counted in the composite outcome if it occurred while on Impella 5.5 support or after elective withdraw of care that was expected to precipitate death. This did not include patients who survived to Impella 5.5 removal and later unexpectedly died. Stroke and dialysis events that occurred either before or after Impella 5.5 support were not included. Secondary outcomes assessed separately from the composite outcome included transition to durable LVAD or heart transplant from Impella 5.5, overall hospital mortality, and the individual components of the composite outcome.

Statistical Analysis

Analyses used SAS, version 9.4 (SAS Institute) and R, version 3.3.2 (R Foundation for Statistical Computing). Continuous variables are

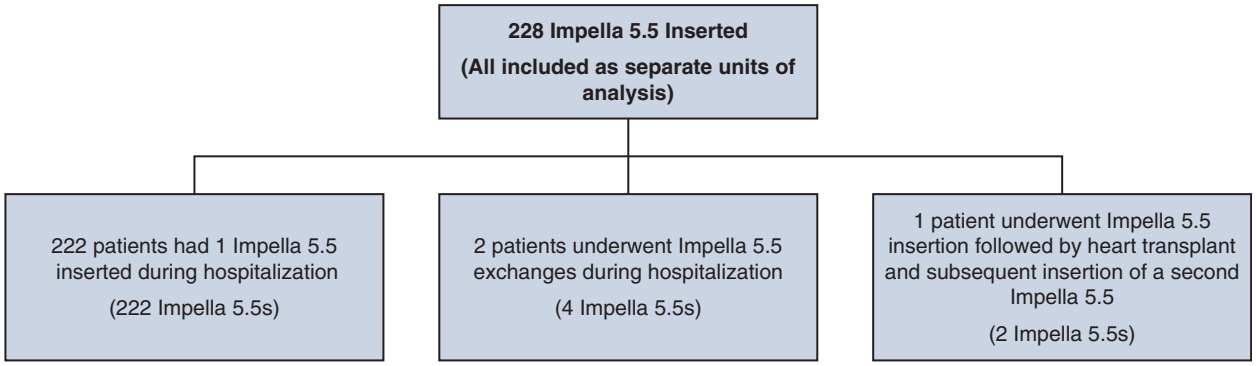


FIGURE 1. Patient cohort. Patients who underwent Impella 5.5 insertion during study time frame at our center.

reported as mean ± standard deviation when normally distributed or medians with 15th/85th percentiles equivalent to one standard deviation when non-normally distributed and compared using Wilcoxon rank sum tests. Categorical data are summarized using frequencies and percentages and compared using χ^2 tests or Fisher exact tests when frequency ≤5.

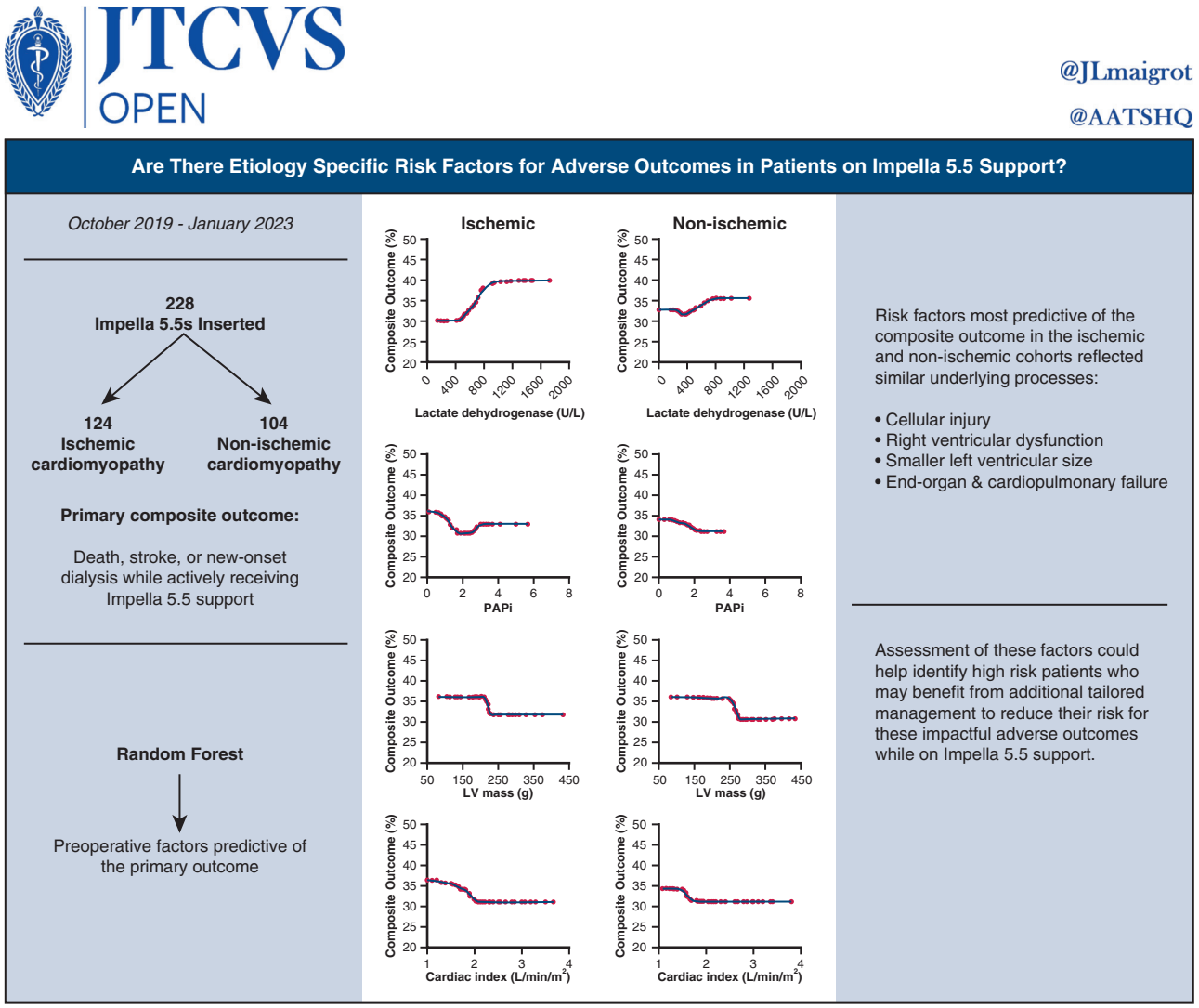


FIGURE 2. Risk factors for a composite outcome of death, stroke, or new-onset dialysis while actively receiving Impella 5.5 support were analyzed for patients with ischemic and nonischemic cardiomyopathy. *PAPi*, Pulmonary artery pulsatility index; *LV*, left ventricular.

TABLE 1. Patient characteristics

Variable	Ischemic (N = 124) Mean ± SD, median (15th, 85th percentiles), n (%)	Nonischemic (N = 104) Mean ± SD, median (15th, 85th percentiles), n (%)	*P*
Indications			
Cardiogenic shock	77 (62)	73 (70)	.20
Acute myocardial infarction	34 (27)	0 (0)	<.01
Decompensated heart failure	28 (23)	56 (54)	<.01
Postcardiotomy	15 (12)	7 (6.7)	.17
Myocarditis	0 (0)	5 (4.8)	.01
Posttransplant graft dysfunction	0 (0)	2 (1.9)	.12
Posttransplant graft rejection	0 (0)	2 (1.9)	.12
Traumatic cardiac injury	0 (0)	1 (1.0)	.27
Assisted cardiac intervention	47 (38)	31 (30)	.20
Percutaneous coronary intervention	3 (2.4)	0 (0)	.11
Ventricular tachycardia ablation	13 (10)	17 (16)	.19
Cardiac surgery	31 (25)	14 (13)	.03
Intermacs profile			.03
1	29 (23)	35 (34)	
2	36 (29)	37 (36)	
3	14 (11)	7 (6.7)	
4-7	45 (36)	25 (24)	
SCAI stage			<.01
Stage A	38 (31)	25 (24)	
Stage B	10 (8.1)	0 (0)	
Stage C	15 (12)	16 (15)	
Stage D	56 (45)	48 (46)	
Stage E	5 (4.0)	15 (14)	
Demographics			
Age, y	65 (57, 75)	56 (36, 70)	<.01
Female	22 (18)	21 (20)	.64
Race			<.01
White	99 (80)	68 (65)	
Black	11 (8.9)	30 (29)	
Asian	0 (0)	1 (2.0)	
Multi	5 (4.0)	4 (3.8)	
Unknown	9 (7.3)	1 (1.0)	
Body mass index, kg/m^2	30 ± 6	29 ± 6	.70
Comorbidities			
Diabetes	55 (44)	22 (21)	<.01
Hypertension	85 (69)	52 (50)	<.01
Coronary artery disease	120 (97)	20 (19)	<.01
Previous percutaneous coronary intervention	59 (48)	5 (4.8)	<.01
Atrial fibrillation	39 (31)	42 (40)	.16
History of ventricular tachycardia/fibrillation	27 (22)	30 (29)	.22
Presence of ICD	35 (28)	60 (58)	<.01
Chronic obstructive pulmonary disease	17 (14)	8 (7.7)	.15
Peripheral vascular disease	20 (16)	4 (3.8)	<.01
Cardiac arrest	27 (22)	18 (17)	.40
History of previous cardiac surgery	30 (24)	15 (14)	.07
History of stroke	18 (15)	13 (13)	.66
Shock liver*	21 (17)	16 (15)	.75
Mechanical ventilation	45 (36)	31 (30)	.30
Cardiac arrest	27 (22)	18 (17)	.40
Transferred from outside hospital	82 (66)	55 (53)	.04

(Continued)

TABLE 1. Continued

Variable	Ischemic (N = 124) Mean ± SD, median (15th, 85th percentiles), n (%)	Nonischemic (N = 104) Mean ± SD, median (15th, 85th percentiles), n (%)	*P*
Device strategy			.
Bridge to advanced therapy	11 (8.9)	19 (18)	.04
Bridge to decision	26 (21)	31 (30)	.12
Bridge to recovery	87 (70)	54 (52)	<.01

*Ischemic hepatitis (pre-Impella ALT or AST >1000 U/L). *SD*, Standard deviation; *Intermacs*, Interagency Registry for Mechanically Assisted Circulatory Support; *SCAI*, Society for Cardiovascular Angiography and Intervention; *ICD*, implantable cardioverter-defibrillator.

Risk Factors

Random forest classification for imbalanced data was used to identify preoperative factors predictive of the composite outcome.[7] Random forest is a nonparametric, statistical ensemble method that uses all variables and makes no distributional or functional (linear or nonlinear) or interaction-effects assumptions about covariate relationships to the response. Forests were grown using 5000 regression trees with 10 randomly selected variables at each split from those in Table E1. Missing data were imputed "on the fly" as part of growing the forest object.[8] Random forest variable importance (VIMP) was used to rank variables in relation to reduction in prediction error.[9] The relationships between predicted probability of the composite outcome and risk factors with high VIMP were visualized using partial dependency plots, which describe the risk-adjusted relationship between the covariate of interest and the outcome by integrating out the effects of all other covariates.[10] Values of each continuous risk factor corresponding to the inflection point of the predicted probability of the composite outcome were approximated by visual inspection of the partial dependency plots.

RESULTS

Patient Characteristics

More patients with ICM than with NICM had coronary artery disease and its sequalae, in addition to history of percutaneous coronary intervention (Table 1). Four patients without coronary artery disease developed ICM related to myocardial bridges (n = 2) or iatrogenic injury during previous cardiac surgery (n = 2). Diabetes, hypertension, and peripheral vascular disease were also more prevalent in the ICM cohort. Patients with ICM more often presented initially to outside hospitals and were transferred to Cleveland Clinic for escalation of care. More patients with NICM than ICM had implanted cardioverter-defibrillators.

Most Impella 5.5 devices were inserted for cardiogenic shock. Cardiogenic shock was the indication in 62% of patients with ICM and 70% of those with NICM. All remaining devices were inserted for assisted high-risk cardiac interventions; more patients with ICM underwent Impella 5.5-assisted cardiac operations.

Cardiogenic shock was more often caused by AMI in patients with ICM and decompensated heart failure in those with NICM. More patients with NICM were in Intermacs profile 1 and Society for Cardiovascular Angiography and Interventions stage E than those with ICM. Impella 5.5 devices were also more often inserted for bridge to advanced therapy in patients with NICM and bridge to recovery in patients with ICM; Impella 5.5 use for bridge to decision was similar between cohorts.

Preoperative Evaluations

There were no statistically significant differences between the ICM and NICM cohorts in preoperative cardiac index, PA pressures, or PAPi (Table 2). Preoperative inotrope/vasopressor use was greater in the NICM cohort. Presence of other preoperative tMCS, number days on tMCS before Impella 5.5, and the specific types of tMCS used were not significantly different between cohorts.

Although most patients in both cohorts had a severe grade of preoperative left ventricular (LV) dysfunction, the distribution of LV dysfunction grades was similar between cohorts. However, preoperative LV ejection fraction was lower, and left ventricular end-diastolic diameter (LVEDD) was greater among patients with NICM. Severe right ventricular (RV) dysfunction was also more common in patients with NICM, as were moderate/severe mitral and tricuspid regurgitation. Most preoperative laboratory values were not statistically significantly different between cohorts, but the ICM cohort had greater B-type natriuretic peptide and the ICM cohort had greater troponin.

Outcomes

In patients with ICM, the primary composite outcome of death/stroke/new-onset dialysis while actively receiving Impella 5.5 support occurred in 42 (34%) patients (Table 3). Mortality occurred in 21 (17%), stroke occurred in 12 (9.7%), and new-onset dialysis was initiated in 23 (19%) patients while actively receiving Impella 5.5 support. Among those who survived past Impella 5.5 support, 21 (17%) transitioned to durable LVAD or heart transplant, whereas the others were weaned without advanced therapies. Mortality after Impella 5.5 removal occurred in 9 patients; hospital mortality occurred for 30 (34%) patients total in the ICM cohort.

In patients with NICM, the primary composite outcome occurred in 35 (34%) patients. Mortality occurred in 21 (20%), stroke occurred in 3 (2.9%), and new-onset dialysis was initiated in 24 (23%) patients while actively receiving

TABLE 2. Preoperative assessments

Variable	Ischemic (N = 124) N	Ischemic (N = 124) Mean ± SD, median (15th, 85th percentiles), n (%)	Nonischemic (N = 104) N	Nonischemic (N = 104) Mean ± SD, median (15th, 85th percentiles), n (%)	*P*
Hemodynamics					
Cardiac index, L*min^{-1}*m^{-2}	93	2.2 ± 0.8	83	2.0 ± 0.7	.10
PA systolic pressure, mm Hg	109	46 ± 12	97	48 ± 17	.46
PA mean pressure, mm Hg	109	33 ± 9.1	97	35 ± 11	.16
Central venous pressure	91	14 ± 6.8	82	16 ± 7.5	.07
Pulmonary artery pulsatility index	88	1.5 (0.7, 3.7)	82	1.3 (0.7, 2.7)	.16
Hemodynamic support					
Inotropes/vasopressors	124	50 (40)	104	60 (58)	<.01
Temporary mechanical circulatory support	124	63 (51)	104	52 (50)	.90
Intra-aortic balloon pump	63	30 (48)	52	32 (62)	.14
ECMO	63	25 (40)	52	16 (31)	.32
Impella	63	24 (38)	52	12 (23)	.08
TandemHeart	63	1 (1.6)	52	0 (0)	.36
Days on temporary mechanical circulatory support	63	2.0 (1.0, 7.0)	52	1.0 (1.0, 8.1)	.23
Echocardiography					
LV ejection fraction, %	120	23 ± 12	99	19 ± 12	<.01
LV systolic dysfunction	122		104		.17
Moderate		26 (21)		12 (12)	
Severe		91 (75)		88 (85)	
RV systolic dysfunction	121		103		.03
Moderate		25 (21)		20 (19)	
Severe		32 (26)		46 (45)	
LV end-diastolic diameter, cm	96	5.8 ± 1.1	86	6.6 ± 1.4	<.01
Left ventricular mass, g	76	228 ± 79	70	271 ± 110	.01
Aortic regurgitation	119		101		.11
Moderate		4 (3.4)		5 (5)	
Severe		1 (0.8)		5 (5)	
Mitral regurgitation	122		101		<.01
Moderate		28 (23)		34 (34)	
Severe		13 (11)		22 (22)	
Tricuspid regurgitation	121		101		<.01
Moderate		19 (16)		33 (33)	
Severe		6 (5)		11 (11)	
Laboratory					
Albumin, g/dL	123	3.4 (2.4, 4.1)	104	3.6 (2.8, 4.1)	.09
Alanine aminotransferase, U/L	123	3.8 (2.6, 32)	104	3.8 (3, 21)	.52
Aspartate aminotransferase, U/L	123	35 (19, 222)	104	31 (18, 123)	.31
Lactate dehydrogenase, U/L	56	345 (192, 1470)	52	295 (217, 817)	.56
Bilirubin, mg/dL	123	0.8 (0.4, 1.9)	104	0.8 (0.4, 2.5)	.47
Creatinine, mg/dL	124	1.4 (0.9, 2.8)	104	1.4 (1.0, 2.4)	.85
B-type natriuretic peptide, pg/mL	101	3270 (630, 16,600)	91	6260 (959, 24,300)	.02
Lactate, mmol/L	122	1.4 (0.8, 2.7)	102	1.3 (0.8, 3.1)	.45
Platelets, $\times 10^9$/L	124	171 (97, 250)	104	170 (89, 266)	.89
Troponin (*upper limit of normal)	83	15 (1.2, 282)	50	2.1 (0.5, 22)	<.01

Fick cardiac index used when available; otherwise thermodilution is used. *SD*, Standard deviation; *PA*, pulmonary artery; *ECMO*, extracorporeal membrane oxygenation; *LV*, left ventricle; *RV*, right ventricle.

Impella 5.5 support. Among those who survived past Impella 5.5 support, 34 (33%) transitioned to durable LVAD or heart transplant and the others were weaned without advanced therapies. Mortality after Impella 5.5 removal occurred in 7 patients; hospital mortality occurred for 28 (27%) patients total in the NICM cohort.

TABLE 3. Patient outcomes

Variable	Ischemic (N = 124) n (%)	Nonischemic (N = 104) n (%)
Primary composite outcome	42 (34)	35 (34)
Death on support	21 (17)	21 (20)
Stroke on support	12 (9.7)	3 (2.9)
New-onset dialysis on support	23 (19)	24 (23)
Weaned without advanced therapies	82 (66)	47 (45)
Transitioned to durable LVAD/heart transplant	21 (17)	34 (33)
Device exchanged	0 (0)	2 (1.9)
Total hospital mortality	30 (34)	28 (27)

LVAD, Left ventricular assist device.

Risk Factors

Among patients with ICM, the variables most predictive of the composite outcome, ranked by VIMP, were greater levels of lactate dehydrogenase (LDH), preoperative mechanical ventilation, lower PAPi, lower low-density lipoprotein, lower LV mass, lower cardiac index, lower PA systolic pressure, preoperative cardiac arrest, lower LVEDD, and lower platelets (Figure 3). Shapes of the relationships of continuous risk factors to the composite outcome varied but indicated approximately that LDH >∼500 U/L, PAPi <∼2, low density lipoprotein <∼75 mg/dL, LV mass <∼250 g, cardiac index <∼2 L min^{-1} m^{-2}, PA systolic pressure <∼40 mm Hg, LVEDD <∼5 cm, and platelets <∼150,000/μL corresponded to inflection points in the predicted probabilities of the composite outcome.

Among patients with NICM, the variables most predictive of the composite outcome, ranked by VIMP, were greater troponin, lower albumin, greater lactate, greater white blood cell count, lower LV mass, presenting in Intermacs profile 1, greater central venous pressure, lower cardiac index, greater LDH, and lower PAPi (Figure 4). Shapes of the relationships of continuous risk factors to the composite outcome varied but indicated approximately that troponin >∼10× upper limit of normal, albumin <∼3.5 g/dL, lactate >∼1.5 mmol/L, white blood cells >∼10,000/μL, LV mass <∼250 g, central venous pressure >∼15 mm Hg, cardiac index <∼1.5 L min^{-1} m^{-2}, LDH >∼400 U/L, and PAPi <∼2 corresponded to inflection points in the predicted probabilities of the composite outcome.

DISCUSSION

Principal Findings

We evaluated a large single-center cohort of consecutive patients supported with Impella 5.5 devices and aimed to identify risk factors for major adverse outcomes while actively on support. These events can affect the potential success of overall management programs in which Impella 5.5 is a component. Risk factors reflecting cellular injury, end-organ and cardiopulmonary failure, RV dysfunction, and smaller LV dimensions were most predictive of major adverse outcomes in both cohorts. However, differences were found between etiology cohorts in the importance of these risk factors and the magnitudes of their associations with these outcomes.

Patient Profiles

Differences in the profiles of patients with ICM and NICM who underwent Impella 5.5 insertion emphasize the importance of evaluating etiology-specific risk factors. In patients with ICM, the burdens of coronary artery disease, diabetes, and peripheral artery disease suggest a greater systemic atherosclerotic burden, which has the potential to affect outcomes and may have contributed to more strokes occurring in this cohort. In addition, greater use of Impella 5.5 as a bridge to recovery may reflect underlying pathophysiologic differences, as ICM more often involves discrete lesions that can be revascularized to facilitate recovery.[11]

In comparison, those with NICM often presented in more decompensated states suggestive of end-stage cardiomyopathy. They had lower LV ejection fraction, worse RV dysfunction, greater B-type natriuretic peptide, and more often had implanted cardioverter-defibrillators. They also more often had significant mitral and tricuspid regurgitation with more dilated LVs.[12] Impella 5.5 devices were also more often used as bridge to advanced therapies, which may reflect the natural course of NICM, as it often has minimal potential for native cardiac recovery and may require advanced therapies.[13]

Indications and Device Strategies

Previous single- and multicenter studies have described outcomes of patients supported with Impella 5.5 devices stratified a priori by indication and device strategy.[1,14,15] Although we included indication and device strategy as variables in our models, these were not identified among the most predictive risk factors for adverse outcomes while actively receiving Impella 5.5 support in either cohort. This suggests that risk of adverse outcomes may be more related to the associated degrees of cellular injury, end-organ and cardiopulmonary failure, RV dysfunction and LV size than indication or device strategy. Furthermore, our study provides granular insight into the risk-adjusted relationships between risk factors and the predicted probabilities of a major adverse outcome. Given the potential for significant variation in preoperative clinical status within a specific indication or device strategy group, our results may help inform more precise risk stratification.

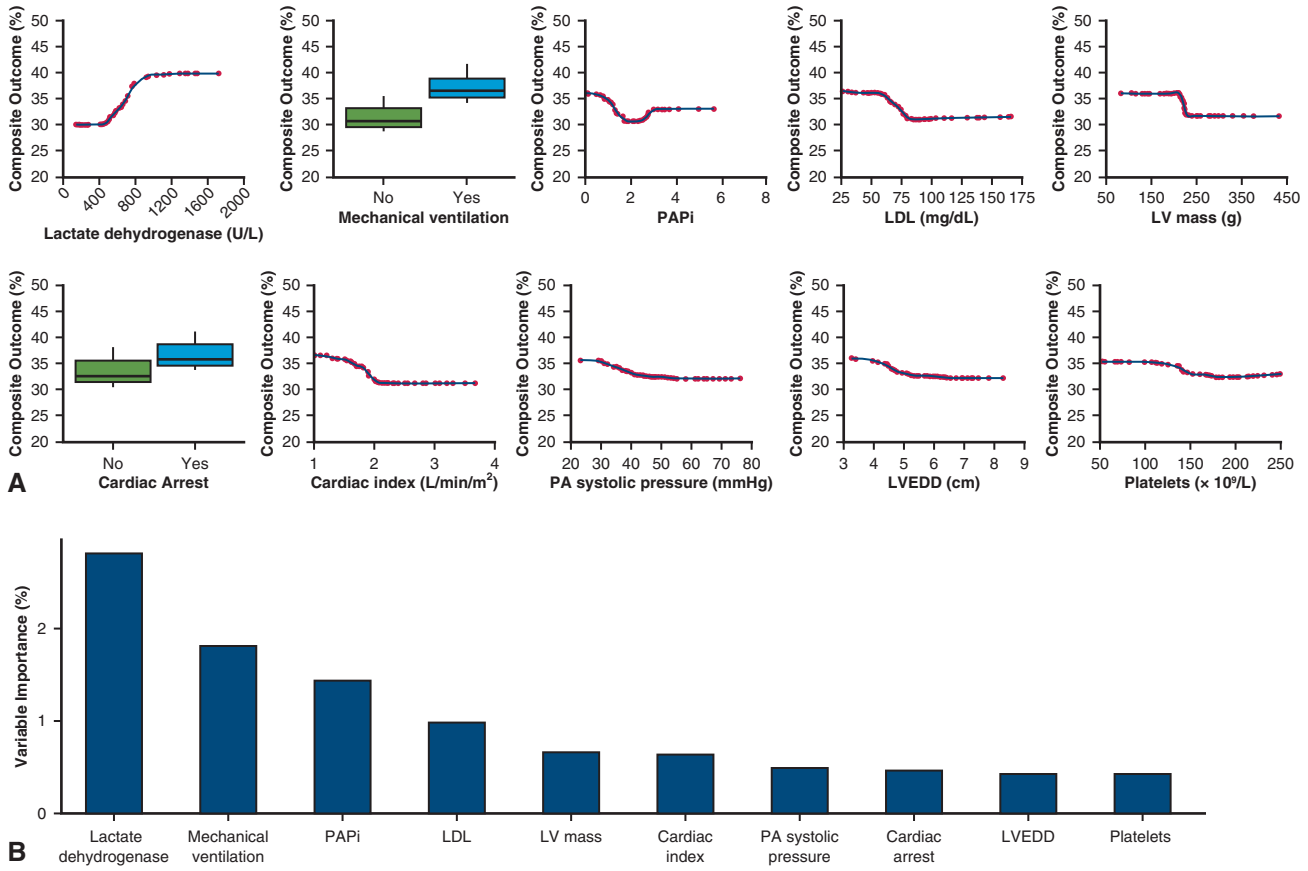


FIGURE 3. Preoperative factors predictive of composite of death, stroke, or new-onset dialysis while actively receiving Impella 5.5 support in patients with ischemic cardiomyopathy. A, Partial dependency plots demonstrating the risk-adjusted relationship between variables and the composite outcome. *Symbols* are risk-adjusted predicted probability of the composite outcome at different values of the continuous covariables. *Solid lines* are smoothed lowest lines of the symbols. *Box-and-whisker plots* depict the predicted probabilities of the composite outcome at different values of categorical covariables, with *whiskers* representing the minimum and maximum values and *boxes* representing the 15th and 85th percentiles of the predicted probabilities. B, Variable importance of the top 10 risk factors for the composite outcome. *PAPi*, Pulmonary artery pulsatility index; *LDL*, low-density lipoprotein; *LV*, left ventricle; *PA*, pulmonary artery; *LVEDD*, left ventricular end diastolic diameter.

Cellular Injury

In both the ICM and NICM cohorts, elevated LDH, which is a marker of systemic and myocardial injury that has been associated with worse outcomes in heart failure patients, was predictive of a major adverse outcome.[16] Specifically in patients with AMI, LDH correlates with the extent of the infarcted myocardium, which is highly associated with outcomes after AMI.[17,18] Elevated LDH can also be a marker of hemolysis, which is a known complication of smaller-sized Impella CP devices used in many patients with AMI cardiogenic shock.[19] Although in our experience, hemolysis typically decreases with upgrade to an Impella 5.5, it has the potential to affect morbidity and mortality.[19] Thus, future studies with more granular data for specific markers of hemolysis are needed to further understand these findings.

Among patients with NICM, increasing preoperative troponin was the most predictive risk factor. Elevated troponin can develop as the result of cardiomyocyte damage, which occurs in NICM as the result of LV dilation and dysfunction that cause myocardial ischemia, and has been identified an independent risk factor for hospital mortality in patients with NICM.[20] In addition, elevated preoperative lactate, a marker of worsening systemic hypoperfusion associated with increased hospital mortality among patients with heart failure, was identified as a top risk factor.[21] Notably, a mild increase in lactate >∼1.5 mmol/L was more predictive of the composite outcome. Although not a significantly elevated value, subtle elevations in lactate before overt signs of hypoperfusion have been previously associated with worse outcomes in patients with heart failure.[22]

Although different in underlying etiology, both ICM and NICM can result in significant hemodynamic compromise. Even when Impella 5.5 support is initiated to restore perfusion, insults that occurred before escalation of support appear to have a major effect on outcomes across etiologies. Thus, timely identification of patients at risk for further deterioration is critical, as it may facilitate earlier escalation to Impella 5.5 support before worsening cellular injury.

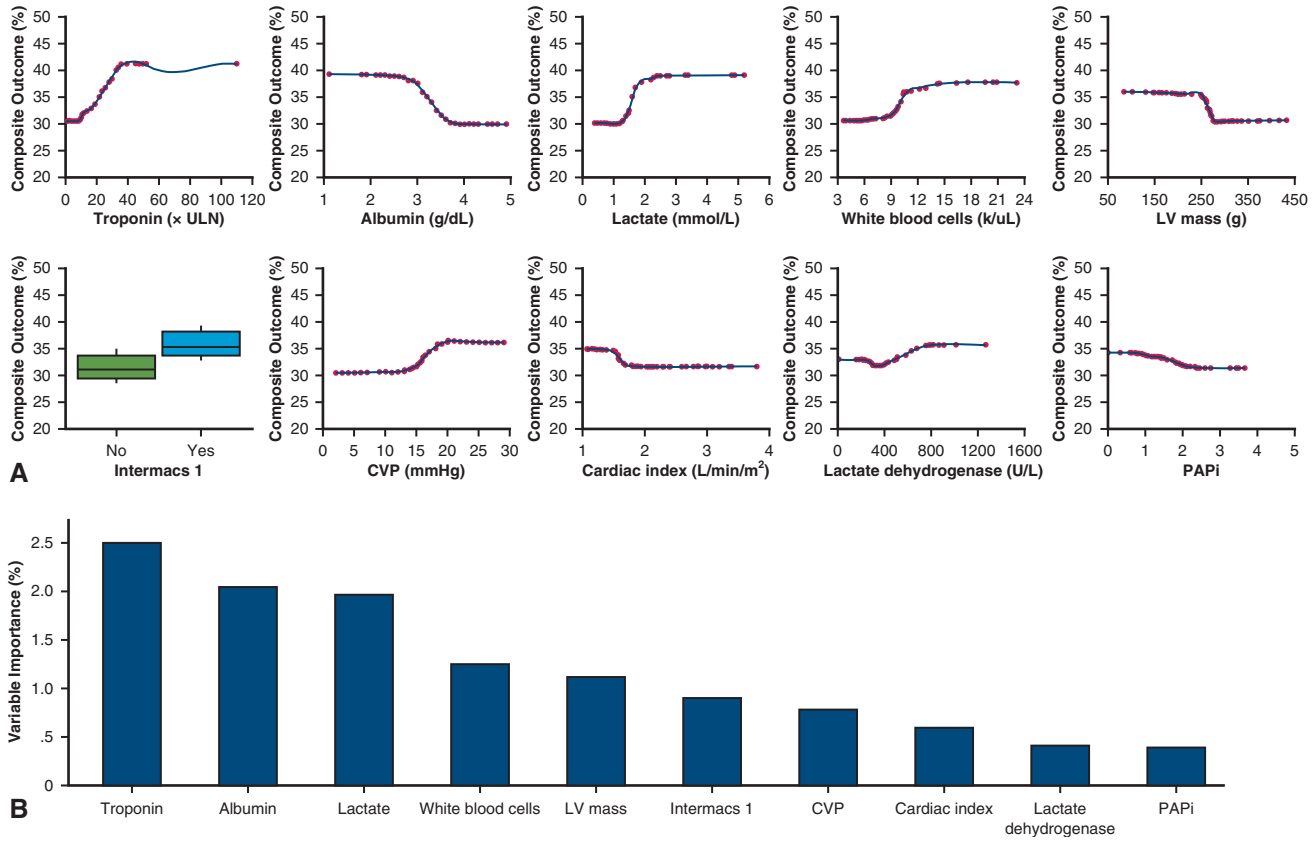


FIGURE 4. Preoperative factors predictive of composite of death, stroke, or new-onset dialysis while actively receiving Impella 5.5 support in patients with nonischemic cardiomyopathy. A, Partial dependency plots demonstrating the risk-adjusted relationship between variables and the composite outcome. *Symbols* are risk-adjusted predicted probability of the composite outcome at different values of the continuous covariables. *Solid lines* are smoothed lowest lines of the symbols. *Box-and-whisker plots* depict the predicted probabilities of the composite outcome at different values of categorical covariables, with *whiskers* representing the minimum and maximum values and *boxes* representing the 15th and 85th percentiles of the predicted probabilities. B, Variable importance of the top 10 risk factors for the composite outcome. *LV*, Left ventricle; *Intermacs*, Interagency Registry for Mechanically Assisted Circulatory Support; *CVP*, central venous pressure; *PAPi*, pulmonary artery pulsatility index.

End-Organ and Cardiopulmonary Failure

Features of worsening end-organ dysfunction were predictive of a major adverse outcome in both the ICM and NICM cohorts. Among patients with ICM this included thrombocytopenia, which is correlated with declining hepatic and renal function, can be a result of hemolysis, and is associated with worse survival in cardiogenic shock.[23] Specifically, among patients with AMI, thrombocytopenia is associated with increased risk of ischemic stroke.[24] In addition, although not evaluated directly in the composite outcome, thrombocytopenia increases bleeding risk.[25] These factors all may contribute to increased morbidity and mortality on Impella 5.5.

Among patients with NICM, decreasing albumin was an important risk factor. Hypoalbuminemia in patients with heart failure is multifactorial and involves malnutrition, inflammation, hepatic dysfunction, and renal failure in the setting of malperfusion.[26] It can develop secondary to both chronic heart failure and acute cardiogenic shock and has been associated with increased mortality and morbidity in both settings.[27]

In addition, in both patients with ICM and NICM, lower cardiac index was identified as an important risk factor. Notably, average cardiac index was only mildly less than normal in both cohorts, suggesting that there may be a more high-risk subset of these patients with more diminished cardiac indices. These may be patients who presented in more decompensated states or continued to have an insufficient cardiac index despite other pharmacologic and tMCS therapies. Patients who decline despite initial therapy and require escalation of support have been shown to have worse outcomes.[28] In addition, more severe preoperative cardiac dysfunction potentially increases the degree of cellular injury and end-organ failure, which was also predictive of adverse outcomes on Impella 5.5.

The importance of mechanical ventilation and preoperative cardiac arrest as risk factors in patients with ICM emphasizes the impact of acute cardiopulmonary failure on

outcomes in this cohort. In patients presenting with AMI cardiogenic shock, requirement for mechanical ventilation is associated with a 3-fold increase in mortality.[29] In addition, preoperative cardiac arrest has been associated with a 6-fold increase in 30-day mortality even after successful revascularization in patients with AMI in cardiogenic shock.[30]

Similarly, in patients with NICM, severe preoperative acuity as characterize by Intermacs profile 1 was predictive of the composite outcomes. Among patients with ICM in cardiogenic shock requiring tMCS, presentation in Intermacs profile 1 is associated with worse outcomes compared to less acute profiles.[31] Despite differences in preoperative presentations, patients with ICM and NICM may have worse outcomes on Impella 5.5 when presenting with increased acuity and end-organ dysfunction. Evaluation of these risk factors in candidates for Impella 5.5 insertion may help identify patients who may and may not benefit from escalation of support.

Right Ventricular Dysfunction

In both the ICM and NICM cohorts, markers of RV dysfunction were identified as important risk factors. These included decreasing PAPi and PA systolic pressure and increasing central venous pressure. Worsening RV dysfunction may represent more advanced end-stage cardiomyopathy and is associated with morbidity and mortality across a variety of heart failure etiologies.[32,33] Despite preoperative differences suggesting that patients with NICM presented in more decompensated states, these findings indicate worsening biventricular failure and progression of end-stage cardiomyopathy may portend worse outcomes across etiologies. Thus, preoperative evaluation of RV function may be critical to improving patient selection and more accurately anticipating patient trajectories on Impella 5.5.

Left Ventricular Dimensions

Across etiologies, smaller LV dimensions, as denoted by lower LVEDD and LV mass, also predicted the composite outcome. A smaller LV cavity may result in less efficient and productive cardiac output from Impella 5.5 due to predisposition to suction events and obstruction of the inflow by the subvalvular apparatus or LV walls.[34] Although smaller LV dimensions are not typically considered a risk factor in patients with cardiogenic shock, this may be an important factor to consider, specifically in those on an Impella 5.5. Thus, preoperative evaluation of LV dimensions on echocardiography is critical. In patients with small LV chambers, regular assessment for proper device positioning is important to mitigate potential for obstruction.

Strengths and Limitations

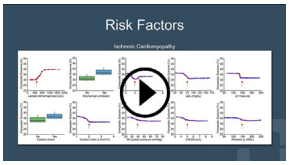
Key strengths of this study are its inclusion of a large, all-comers patient population that is reflective of day-to-day clinical practice and its use of robust statistical methods with consideration of a large set of preoperative variables as potential risk factors. However, this study is limited by its single-center retrospective nature and is subject to potential selection bias. We also only evaluated risk factors for a composite outcome. Although beyond the scope of this study, the individual components, and other complications on Impella 5.5 remain important (Appendix E1). In addition, we only studied events occurring while actively receiving Impella 5.5 support. Although we focused on events on support that have the potential to affect downstream success of overall management programs that include Impella 5.5, future studies evaluating long-term trajectories of these patients are also needed. Furthermore, some variables, including rarer indications for Impella 5.5, had low patient counts and were not included in the random forest models. However, preoperative variables included in the models may help account for differences in preoperative clinical status between these rarer indications. Moreover, NICM was defined as a combination of multiple more specific etiologies. Although this was necessary, given the small sample size in most NICM subtypes, differences underlying various etiologies of NICM may contribute to differences in risk factors and outcomes.

CONCLUSIONS

Analysis of risk factors for major adverse outcomes occurring during tMCS with an Impella 5.5, which can affect the overall success of management programs involving this device, suggests that the degree of cellular injury, end-organ and cardiopulmonary failure, RV dysfunction, and smaller LV dimensions were predictors of these outcomes in both patients with ICM and NICM. However, the quantitative effects of these predictors were etiology specific. These findings may help identify high-risk patients who may benefit from additional tailored management while on Impella 5.5 support to reduce their risk for these impactful adverse events.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/etiology-specific-risk-factors-7059.



Conflict of Interest Statement

Dr Soltesz has been a speaker for Abiomed and provided training for Abbott. Dr Tong has been a consultant and speaker for Abbott and Abiomed. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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References

1. Ramzy D, Soltesz EG, Silvestry S, Daneshmand M, Kanwar M, D'Alessandro DA. Improved clinical outcomes associated with the Impella 5.5 compared to the Impella 5.0 in contemporary cardiogenic shock and heart failure patients. *J Heart Lung Transplant*. 2023;42(5):553-557. https://doi.org/10.1016/j.healun.2023.01.011
2. Yang S, Liu Z, Hu Y, et al. A novel risk model for mortality and hospitalization following cardiac resynchronization therapy in patients with non-ischemic cardiomyopathy: the alpha-score. *BMC Cardiovasc Disord*. 2020;20:205. https://doi.org/10.1186/s12872-020-01460-x
3. Kusunose K, Obuchowski NA, Gillinov M, et al. Predictors of mortality in patients with severe ischemic cardiomyopathy undergoing surgical mitral valve intervention. *J Am Heart Assoc*. 2017;6(11):e007163. https://doi.org/10.1161/JAHA.117.007163
4. Felker GM, Thompson RE, Hare JM, et al. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. *N Engl J Med*. 2000;342(15):1077-1084. https://doi.org/10.1056/NEJM200004133421502
5. Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock. *Catheter Cardiovasc Interv*. 2019;94(1):29-37. https://doi.org/10.1002/ccd.28329
6. Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. *J Heart Lung Transplant*. 2009;28(6):535-541. https://doi.org/10.1016/j.healun.2009.02.015
7. Ishwaran H, Kogalur UB. Fast Unified Random Forests for Survival, Regression, and Classification (RF-SRC), R package, version 3.2.1; 2023. Accessed February 5, 2024. http://cran.r-project.org/package=randomForestSRC
8. Tang F, Ishwaran H. Random forest missing data algorithms. *Stat Anal Data Min*. 2017;10(6):363-377. https://doi.org/10.1002/sam.11348
9. Ishwaran H, Lu M. Standard errors and confidence intervals for variable importance in random forest regression, classification, and survival. *Stat Med*. 2019;38(4):558-582. https://doi.org/10.1002/sim.7803
10. Friedman JH. Greedy function approximation: a gradient boosting machine. *Ann Stat*. 2001;29(5):1189-1232. https://doi.org/10.1214/aos/1013203451
11. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med*. 2016;374(16):1511-1520. https://doi.org/10.1056/NEJMoa1602001
12. van der Bijl P, Khidir M, Ajmone Marsan N, et al. Effect of functional mitral regurgitation on outcome in patients receiving cardiac resynchronization therapy for heart failure. *Am J Cardiol*. 2019;123(1):75-83. https://doi.org/10.1016/j.amjcard.2018.09.020
13. Pueschner A, Chattranukulchai P, Heitner JF, et al. The prevalence, correlates, and impact on cardiac mortality of right ventricular dysfunction in nonischemic cardiomyopathy. *JACC Cardiovasc Imaging*. 2017;10(10 pt B):1225-1236. https://doi.org/10.1016/j.jcmg.2017.06.013
14. Schumer EM, Bai YZ, Kotkar KD, et al. Surgically implanted endovascular, micro axial left ventricular assist device: a single institution study. *J Thorac Cardiovasc Surg Tech*. 2023;23:63-71. https://doi.org/10.1016/j.xjtc.2023.10.012
15. Funamoto M, Kunavarapu C, Kwan MD, Matsuzaki Y, Shah M, Ono M. Single center experience and early outcomes of Impella 5.5. *Front Cardiovasc Med*. 2023;10:1018203. https://doi.org/10.3389/fcvm.2023.1018203
16. Yamaguchi S, Abe M, Arakaki T, Arasaki O, Shimabukuro M. Prognostic value of lactate dehydrogenase for mid-term mortality in acute decompensated heart failure: a comparison to established biomarkers and brain natriuretic peptide. *Heart Lung Circ*. 2020;29(9):1318-1327. https://doi.org/10.1016/j.hlc.2019.11.013
17. Elsman P, Zijlstra F, Miedema K, et al. The predictive value of cumulative lactate dehydrogenase release within the first 72 h of acute myocardial infarction in patients treated with primary angioplasty. *Ann Clin Biochem*. 2004;41(pt 2):142-148. https://doi.org/10.1258/000456304322880041
18. Stone GW, Selker HP, Thiele H, et al. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. *J Am Coll Cardiol*. 2016;67(14):1674-1683. https://doi.org/10.1016/j.jacc.2016.01.069
19. Van ECJ, Gramegna M, Baldetti L, et al. Management of bleeding and hemolysis during percutaneous microaxial flow pump support. *JACC: Cardiovasc Interv*. 2023;16(14):1707-1720. https://doi.org/10.1016/j.jcin.2023.05.043
20. Gao W, Zhang M, Song Y, et al. Different expression and prognostic value of troponin in ischemic cardiomyopathy and non-ischemic dilated cardiomyopathy. *Eur J Med Res*. 2023;28(1):220. https://doi.org/10.1186/s40001-023-01169-5
21. Kawase T, Toyofuku M, Higashihara T, et al. Validation of lactate level as a predictor of early mortality in acute decompensated heart failure patients who entered intensive care unit. *J Cardiol*. 2015;65(2):164-170. https://doi.org/10.1016/j.jjcc.2014.05.006
22. Zymliński R, Biegus J, Sokolski M, et al. Increased blood lactate is prevalent and identifies poor prognosis in patients with acute heart failure without overt peripheral hypoperfusion. *Eur J Heart Failure*. 2018;20(6):1011-1018. https://doi.org/10.1002/ejhf.1156
23. Lee HH, Hong SJ, Ahn CM, et al. Clinical implications of thrombocytopenia at cardiogenic shock presentation: data from a multicenter registry. *Yonsei Med J*. 2020;61(10):851-859. https://doi.org/10.3349/ymj.2020.61.10.851
24. Rubinfeld GD, Smilowitz NR, Berger JS, Newman JD. Association of thrombocytopenia, revascularization, and in-hospital outcomes in patients with acute myocardial infarction. *Am J Med*. 2019;132(8):942-948.e5. https://doi.org/10.1016/j.amjmed.2019.04.003
25. Wang TY, Ou FS, Roe MT, et al. Incidence and prognostic significance of thrombocytopenia developed during acute coronary syndrome in contemporary clinical practice. *Circulation*. 2009;119(18):2454-2462. https://doi.org/10.1161/CIRCULATIONAHA.108.827162
26. Arques S, Ambrosi P. Human serum albumin in the clinical syndrome of heart failure. *J Card Fail*. 2011;17(6):451-458. https://doi.org/10.1016/j.cardfail.2011.02.010
27. Jäntti T, Tarvasmäki T, Harjola VP, et al. Hypoalbuminemia is a frequent marker of increased mortality in cardiogenic shock. *PLoS One*. 2019;14(5):e0217006. https://doi.org/10.1371/journal.pone.0217006
28. Thayer KL, Zweck E, Ayouty M, et al. Invasive hemodynamic assessment and classification of in-hospital mortality risk among patients with cardiogenic shock. *Circ Heart Failure*. 2020;13(9):e007099. https://doi.org/10.1161/CIRCHEARTFAILURE.120.007099
29. Pesaro AEP, Katz M, Katz JN, et al. Mechanical ventilation and clinical outcomes in patients with acute myocardial infarction: a retrospective observational study. *PLoS One*. 2016;11(3):e0151302. https://doi.org/10.1371/journal.pone.0151302
30. Sonoda T, Wada H, Ogita M, et al. Clinical features and predictors of outcome in patients with acute myocardial infarction complicated by out-of-hospital cardiac arrest. *BMC Cardiovasc Disord*. 2022;22(1):185. https://doi.org/10.1186/s12872-022-02628-3
31. Lim HS, Ranasinghe A, Quinn D, Chue C, Mascaro J. Outcomes of temporary mechanical circulatory support in cardiogenic shock due to end-stage heart failure. *J Intensive Care Soc*. 2022;23(2):170-176. https://doi.org/10.1177/1751143720988706
32. Polak JF, Holman BL, Wynne J, Colucci WS. Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. *J Am Coll Cardiol*. 1983;2(2):217-224. https://doi.org/10.1016/s0735-1097(83)80156-9
33. Ghio S, Gavazzi A, Campana C, et al. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. *J Am Coll Cardiol*. 2001;37(1):183-188. https://doi.org/10.1016/s0735-1097(00)01102-5
34. Balthazar T, Van Mieghem NM, Raes M, Van Loo I, Verbrugge FH. Short-term percutaneous mechanical circulatory support: no promise without positioning. *Eur Heart J Acute Cardiovasc Care*. 2023;12(12):869-877. https://doi.org/10.1093/ehjacc/zuad097

Key Words: temporary mechanical circulatory support, ischemic cardiomyopathy, nonischemic cardiomyopathy

APPENDIX 1. CLEVELAND CLINIC MANAGEMENT OF THE IMPELLA 5.5

Prophylactic Impella 5.5 Support

In patients with reduced preoperative or preprocedural left ventricular function, we often consider prophylactic Impella 5.5 support. Our approach to evaluation of these patients has been previous published but in summary focuses on evaluation of the patient's heart failure history, comorbidities, invasive hemodynamic measurements, and response to preoperative optimization.[E1,E2]

Our center has also previous published our experience with the prophylactic use of Impella for patients undergoing high-risk ventricular tachycardia ablation.[E3] Generally, we consider this strategy for patients at high risk of periprocedural acute hemodynamic decompensation and adverse outcomes due to their burden of cardiopulmonary disease and/or a high anticipated burden of periprocedural ventricular tachycardia storm.

Prophylactic use of Impella 5.5 in patients undergoing nonemergent high-risk percutaneous coronary intervention is rare (n = 3), but typically this is indicated when an Impella CP would not provide sufficient hemodynamic support, or the patient has peripheral vascular access issues that complicate Impella CP insertion. These decisions are made on a patient-by-patient basis by our multidisciplinary team.

IMPELLA 5.5 INSERTION TECHNIQUE

We routinely perform Impella 5.5 insertions in an operating room with fluoroscopy and transesophageal echocardiography capabilities. The device is most often inserted via the right axillary artery but can also be inserted via the left axillary artery or direct aortic cannulation. Typically, the right axillary artery is exposed through the deltopectoral groove. The artery is then encircled proximally and distally with vessel loops and heparin is administered for an activated clotting time >250 seconds. The artery is clamped proximally and distally and an arteriotomy is made followed by anastomosis of a 10-mm Dacron graft. The graft is stretched and cut to 18 cm in length and the sheath is inserted to the end of the graft and secured with the clips provided.

Using a combination of fluoroscopy and transesophageal echocardiography, a 5-Fr diagnostic catheter with a 0.035-inch guidewire is inserted through the sheath into the graft and passed retrograde into the ascending aorta and across the aortic valve. The 0.035-inch guidewire is then exchanged over the catheter with a 0.018-inch stiff guidewire. The Impella 5.5 catheter is then loaded onto the guidewire and fully advanced until the inlet is across the aortic valve in the left ventricle and the outlet sits in the aorta. Correct positioning is again confirmed with echocardiography and fluoroscopy. The graft is clamped, the sheath is then removed, and the graft is cut to a size that is fully inside the axillary incision. The blue positioning hub is then secured to the graft and the device is locked into place. We do not routinely tunnel out a separate incision and instead bring the device out the distal end of the axillary cut-down incision. Following reversal with protamine and hemostasis, the incision is closed in multiple layers with no graft being exposed externally.

COMPLICATIONS DURING IMPELLA 5.5 SUPPORT

Reports of complications associated with Impella 5.5 use have been previously reported in multiple series.[E4-E7] However, in our series of 228 devices, these were the complications encountered. Note that these are not mutually exclusive for a given device/patient. In line with the present study, these events were recorded only if they occurred while actively receiving Impella 5.5 support.

Complication on Impella 5.5 support	No. % of 228
Stroke	15 (6.6%)
Upper-extremity ischemia	12 (5.3%)
Brachial plexus neuropathy (all transient)	12 (5.3%)
Confirmed heparin induced thrombocytopenia	7 (3.1%)
Clinically significant bleeding	70 (31%)
Previous temporary mechanical circulatory support cannulation site	6 (8.6%)
Intracranial	0 (0%)
Gastrointestinal	26 (37%)
Retroperitoneal	3 (4.3%)
Mediastinal	21 (30%)
Axillary incision	24 (34%)
Sepsis	12 (5.3%)
Hemolysis	15 (6.6%)
Device malfunction	7 (3.1%)
Device dislocation into ascending aorta	6 (2.6%)
Axillary re-exploration	26 (11%)
Infection	1 (3.8%)
Hematoma	24 (92%)
Device repositioning	1 (3.8%)

IMPELLA 5.5 WEANING PROTOCOL AND RECOVERY

Although protocols exist for weaning patients on Impella 5.5, it is our experience that in a heterogeneous population of patients, a nuanced, individualized approach to Impella weaning is important to optimize success. We have previously described our general considerations for this process.[E1] We routinely use invasive hemodynamic measurements with a pulmonary artery catheter while on Impella 5.5 support to guide flow reductions on the device. Once the device has been weaned down with acceptable cardiac indices and filling pressures with preservation of end-organ function, the device is removed. Individual clinicians may also use echocardiography to further support clinical decisions.

Recovery on temporary mechanical circulatory support lacks a well-described universally accepted definition. At Cleveland Clinic, we define recovery as successful removal of Impella support without progression to death or requirement for advanced therapy. We realize that this definition does not account for patients that go on to needing subsequent support or later interventions later; however, the difficulties with incorporating those events were another reason why we chose to focus the present manuscript on events only while actively receiving Impella 5.5 support.

Using the aforementioned definition for recovery, patients who died on support or who were bridged to advanced therapies technically "failed" weaning of the device. More granular details of weaning attempts were not collected and documentation of these attempts after reviewing the electronic health record were inconsistent across both time and caregiver.

ALTERNATIVE TEMPORARY CIRCULATORY SUPPORT

Although we occasionally use other temporary mechanical circulatory support devices depending on the patient's specific needs, the main device used for isolated severe left ventricular dysfunction requiring significant circulatory support has been the Impella 5.5 over the study period at our center. This reflects both our extensive institutional experience with microaxial transvalvular devices and our preference for keeping support in these patients' peripheral rather than central (such as a CentriMag), and in the upper body rather than the lower body.

Anecdotally, this allows for earlier extubation and physical rehabilitation and avoids the more invasive central placement of support with its inherent issues as well as helps decrease the complications associated with a patient lying flat with support through the lower body over longer periods of time. If a central temporary left ventricular assist device is being considered in a patient at our institution, often it is due to peripheral access issues (which can be overcome by direct aortic insertion on an Impella 5.5) or a small left ventricular cavity where we feel the device is unlikely to work well (further supported by the results of the present study). The focus of this manuscript is specifically on the population of patients supported with an Impella 5.5, however. We agree that these details provide context to the overall use of Impella 5.5, and we have also added them to Appendix E1.

E-References

E1. Maigrot JLA, Weiss AJ, Tong MZY, Bakaeen F, Soltesz EG. Programmatic approach to patients with advanced ischemic cardiomyopathy: integrating microaxial support into strategies for the modern era. *Artif Organs*. 2024;48(1):6-15. https://doi.org/10.1111/aor.14678

E2. Tong MZY, Weiss AJ, Bakaeen F, Soltesz EG. CABG in failing hearts: a how-to-guide to using modern mechanical support as backup. *Innovations (Phila)*. 2021;16(3):227-230. https://doi.org/10.1177/15569845211016455

E3. Sroubek J, Vajapey R, Sipko JJ, et al. First-in-human experience with Impella 5.0/5.5 for high-risk patients with advanced heart failure undergoing VT ablation. *J Am Coll Cardiol*. 2023;82(5):469-471. https://doi.org/10.1016/j.jacc.2023.05.012

E4. Lewin D, Nersesian G, Lanmüller P, et al. Complications related to the access site after transaxillary implantation of a microaxial left ventricular assist device. *J Heart Lung Transplant*. 2023;42(5):679-687. https://doi.org/10.1016/j.healun.2022.12.018

E5. Schumer EM, Bai YZ, Kotkar KD, et al. Surgically implanted endovascular, micro axial left ventricular assist device: a single institution study. *J Thorac Cardiovasc Surg Tech*. 2023;23:63-71. https://doi.org/10.1016/j.xjtc.2023.10.012

E6. Rock JR, Kos CA, Lemaire A, et al. Single center first year experience and outcomes with Impella 5.5 left ventricular assist device. *J Cardiothorac Surg*. 2022;17(1):124. https://doi.org/10.1186/s13019-022-01871-1

E7. Hong Y, Agrawal N, Hess NR, et al. Outcomes of Impella 5.0 and 5.5 for cardiogenic shock: a single-center 137 patient experience. *Artif Organs*. 2024. https://doi.org/10.1111/aor.14735

TABLE E1. List of preoperative variables considered in random forest model

Demographics: age (years); sex; race; weight (kg); BMI (kg/m^2); BSA (m^2).
Indication for Impella 5.5 support: AMI cardiogenic shock; decompensated heart failure cardiogenic shock; postcardiotomy cardiogenic shock; assisted ventricular tachycardia ablation; assisted cardiac surgery.
Intended device strategy: bridge to decision; advanced therapy; recovery.
Intermacs profile: 1 to 7.
SCAI shock stage: Stage A; Stage B; Stage C; Stage D; Stage E.
Comorbidities: acute shock liver; diabetes; hypertension; coronary artery disease; previous percutaneous coronary intervention; atrial fibrillation; history of ventricular tachycardia/fibrillation; presence of ICD; chronic kidney disease; new-onset hemodialysis; active infection/sepsis; COPD; peripheral vascular disease; history of any previous cardiac surgery; history of stroke; mechanical ventilation; transferred from OSH; Pre-Impella 5.5 cardiac arrest.
Hemodynamics: cardiac index; pulmonary artery (PA) systolic; PA diastolic; PA mean; pulmonary capillary wedge pressure; central venous pressure; mean arterial pressure, pulmonary artery pulsatility index (PAPi). **In patients on preoperative ECMO, cardiac index, PA pressures, and PAPi were not considered, but the random forest models preserved these patients for other variables and events.*
Vasoactive medication: vasopressin; dobutamine; milrinone; epinephrine; norepinephrine.
Temporary MCS preinsertion: IABP; ECMO; Impella (CP, 5.5);
Echocardiography: RV systolic function grade; RV cavity dilation grade; LV inner diameter diastole (cm); LV inner diameter systole (cm); LV end-diastolic volume (mL); LV end-systolic volume (mL); Posterior wall thickness (cm); Intraventricular septal thickness (cm); Ejection fraction (%); LV systolic function grade; LV mass (g); AV regurgitation grade; AV stenosis grade; MV regurgitation grade; MV stenosis grade; TV regurgitation grade. **In patients with another Impella in place preoperatively, LV diameters and volumes were not considered, but the random forest models preserved these patients for other variables and events.*
Laboratory measurements: albumin (g/dL); alanine aminotransferase (U/L); aspartate aminotransferase (U/L); INR; lactate dehydrogenase (U/L); lactate (mmol/L); total bilirubin (mg/dL); BUN (mg/dL); creatinine (mg/dL); hematocrit (%); potassium (mmol/L); sodium (mmol/L); APTT (sec); BNP (pg/mL); LDL-cholesterol (mg/dL); White blood cells (k/μL); Platelets (10^9/L), troponin (ULN-upper limit normalized).
Experience: year of Impella implant (as years since 2019).
Missing value flags: (removed in final models)

BMI, Body mass index; *BSA*, bovine serum albumin; *AMI*, acute myocardial infarction; *Intermacs*, Interagency Registry for Mechanically Assisted Circulatory Support; *SCAI*, Society for Cardiovascular Angiography and Intervention; *ICD*, implantable cardioverter-defibrillator; *COPD*, chronic obstructive pulmonary disease; *OSH*, outside hospital; *ECMO*, extracorporeal membrane oxygenation; *MCS*, mechanical circulatory support; *IABP*, intra-aortic balloon pump; *RV*, right ventricular; *LV*, left ventricular; *AV*, atrioventricular; *MV*, mitral valve; *TV*, tricuspid valve; *INR*, international normalized ratio; *BUN*, blood urea nitrogen; *APTT*, activated partial thromboplastin time; *BNP*, brain natriuretic peptide; *LDL*, low-density lipoprotein; *ULN*, upper limit of normal.