Impella Versus Intra-Aortic Balloon Pump for High-Risk PCI: A Propensity-Adjusted Large-Scale Claims Dataset Analysis

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Impella was approved by the Food and Drug Administration in 2015 for use during high-risk percutaneous coronary interventions (PCIs); however, its safety and efficacy compared with intra-aortic balloon pump (IABP) has not been evaluated in contemporary practice and remains debated. We aimed to compare postapproval outcomes and costs of Impella versus IABP support for high-risk PCI in real-world practice across hospitals in the United States. We identified patients from the Premier Healthcare Database undergoing nonemergent Impella- or IABP-supported high-risk PCI. We used propensity adjustment to control baseline, procedure, and post-PCI medical treatment differences between treatment groups. We included patients undergoing nonemergent single-PCI procedures with either Impella or IABP support and excluded patients presenting with acute ST-elevation myocardial infarction or cardiogenic shock or requiring >1 mechanical support devices during index hospitalization. Outcomes included in-hospital survival, myocardial infarction (MI), cardiogenic shock, stroke, bleeding requiring transfusion, acute kidney injury, index hospitalization length of stay, and costs. From April 2016 to June 2019, a total of 48,179 patients were treated with Impella or IABP mechanical circulatory support at 304 hospitals in the United States. Among these, we identified 2,156 patients undergoing nonemergent high-risk PCI treated with Impella (n = 1,447) or IABP (n = 709). After propensity adjustment, Impella use was associated with improved survival (odds ratio [OR] 1.55, 95% confidence interval [CI] 1.02 to 2.36) and less MI (OR 0.29, 95% CI 0.18 to 0.46) and cardiogenic shock (OR 0.54, 95% CI 0.39 to 0.74). Stroke, bleeding requiring transfusion, and acute kidney injury were similar between groups. In conclusion, this Premier Healthcare Database propensity-adjusted analysis, Impella use during nonemergent high-risk PCI was associated with improved survival and reduced in-hospital MI and cardiogenic shock compared with IABP. **(Am J Cardiol 2022;185:29−36)**

Mechanical circulatory support (MCS) with the intra-aortic balloon pump (IABP) or the microaxial Impella blood pump is frequently used during high-risk percutaneous coronary interventions (PCIs) to maintain hemodynamic stability and enable complete revascularization.[1,2] The Impella ventricular devices can provide up to 3.5 l/min of cardiac output and reduce left ventricular preload and afterload, maintain cardiac power output, and prevent myocardial ischemia.[3−10] The PROTECT II randomized trial demonstrated that Impella 2.5 provided superior hemodynamic support compared with IABP and improved major adverse events at 90 days in the per-protocol population (40% with Impella vs 51% with IABP, p = 0.023).[4] Based on these results, the Food and Drug Administration approved Impella 2.5 in 2015 and Impella CP in 2016 for patients undergoing high-risk PCI. We aimed to evaluate outcomes of nonemergent, mechanical supported, high-risk PCI with IABP compared with Impella since its approval in 2016 in a real-world setting, using a large-scale claims database. Although previous registry-based studies have compared population-wide outcomes[11] and acute myocardial infarction (MI) outcomes,[12] this is the first such study to compare outcomes between Impella and IABP in patients with high-risk PCI.

Methods

We identified patients undergoing MCS with Impella or IABP from the Premier Healthcare Database (PHD), a

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large, real-world, hospital-based, service-level, all-payer database, with more than 700 contributing hospitals from all regions of the United States.[13] Inpatient admissions include over 121 million visits, with more than 10 million annual visits since 2012, representing approximately 25% of annual United States inpatient admissions.[13] PHD contains discharge-level information on International Classification of Diseases (ICD) diagnostic codes, hospital-submitted Current Procedural Terminology, and Healthcare Common Procedure Coding System codes for diagnostic and therapeutic procedures recorded during each admission, in addition to demographic characteristics, co-morbidities, and medications. Hospitalization costs of all billed items, including hospital services, medical procedures, equipment fees, medications, diagnostics, and laboratory tests can be determined from the PHD charge master by the cost-accounting department, administrative records on length of stay (LOS), and discharge status.

We identified patients from the PHD undergoing MCS with Impella or IABP at 304 hospitals in the United States after Impella approval from April 2016 to June 2019 (Supplementary Figure 1). Among those, we included only patients undergoing nonemergent high-risk PCI, identified by ICD Tenth Revision (ICD-10) procedure codes (Supplementary Appendix 1) and compared outcomes based on the type of MCS device (Impella or IABP) used during PCI, identified based on ICD-10 procedures codes (i.e., 5A0221D, 5A0211D, 5A02210, and 5A02110) (Supplementary Appendix 1).

We included patients with nonemergent admissions undergoing a single-PCI procedure with either Impella or IABP support on the day of admission and excluded all admissions coded as emergent. We excluded patients with cardiogenic shock or ST-elevation MI (STEMI) on hospital admission, patients undergoing more than 1 PCI procedure during the admission, requiring multiple MCS devices during index hospitalization, or undergoing PCI and MCS on different days. Although single-PCI procedures were selected to exclude patients returning for PCI complications during the same admission, this may have excluded some high-risk procedures for left main or multivessel disease treatment that were staged during the same hospitalization. This likely excluded some but not most of the left main interventions, which are customarily treated first with MCS, and when staging is required, often it is done during a readmission, and therefore, these patients would be included in the population studied. The patient flowchart with inclusion/exclusion criteria is presented in Supplementary Figure 1. All patient data for this analysis were deidentified and exempt from institutional review board approval requirements.

The clinical outcomes of the study were in-hospital survival, MI, cardiogenic shock, all stroke (including ischemic and hemorrhagic stroke), intracerebral hemorrhage or transient ischemic attack, bleeding requiring transfusion, and acute kidney injury (AKI) (codes included in Supplementary Appendix 2) occurring during the index hospitalization at the PCI site. All clinical outcomes were identified during the hospitalization or discharge but were not coded "present on admission". The use of ICD Ninth Revision and ICD-10 codes to identify co-morbidities and overall diagnoses in administrative datasets have been previously validated.[14,15] Economic outcomes included the index hospital LOS and aggregate costs.

A statistical analysis plan was developed a priori and the analysis was performed by the co-authors, without external input. We compared the clinical outcomes of patients treated with Impella versus IABP. Chi-square or Fisher's exact tests and *t* tests were used to identify baseline differences in demographic and clinical characteristics, and standardized mean differences were calculated.

To address potential confounding, propensity scores were created to control for differences in (1) baseline characteristics, (2) procedure characteristics, and (3) in-hospital medications between the Impella and IABP treatment cohorts. The propensity to be treated with Impella or IABP was estimated using logistic regression based on the following baseline characteristics: age; gender; race; marital status; region; insurer; admission type; hospital teaching status; number of hospital beds; and high-cost co-morbidities present on admission, including diabetes mellitus, congestive heart failure, chronic obstructive pulmonary disease, renal failure, hypertension, smoking, obesity, acute respiratory failure, multivessel PCI, and non-STEMI (NSTEMI). In addition, the propensity score model included the following procedure characteristics: rotational atherectomy; intravascular ultrasound; transradial access, bifurcated lesion; chronic total occlusion; and in-hospital medication use: glycoprotein IIb/IIIa inhibitors, ticagrelor, prasugrel, nonvitamin K antagonist oral anticoagulants, and warfarin. To assess the appropriateness of the propensity model, standardized mean differences were estimated before and after propensity adjustment, distributions of the propensity scores were plotted (Supplementary Figure 2), and the c-statistic of the resulting logistic regression model was calculated.

We analyzed unadjusted and propensity-adjusted outcomes during index hospitalization. The unadjusted categorical outcome variables were assessed using chi-square or Fisher's exact tests and summarized using odds ratios (ORs) and 95% confidence intervals (CIs). Independent-sample *t* tests were used to analyze unadjusted cohort differences in LOS and costs.

Adjusted outcomes were assessed using multivariable logistic regression, whereas LOS and costs were analyzed using linear regression. Doubly robust models were adjusted for the propensity score estimates as well as additional selected baseline covariates present on admission (age, gender, diabetes mellitus, smoking, obesity, multivessel PCI, congestive heart failure, chronic renal failure, NSTEMI, and acute respiratory failure) and summarized as adjusted ORs or adjusted mean differences, along with 95% CIs. The method for propensity score adjustment using doubly robust propensity score-adjusted models was specified a priori. The significance threshold was set at an alpha <0.05, without adjustment for multiplicity. All statistical analyses were performed using SAS Enterprise Guide 7.1 software (SAS Institute Inc., Cary, North Carolina).

To address potential major confounding from the possible miscoding of STEMI and cardiogenic shock as "not present on admission" when it might have been present on admission, we performed 2 sensitivity analysis to assess the robustness of the results by first excluding patients with

Table 1
Demographics and baseline characteristics

Variable	IABP n = 709	Impella n = 1,447	Standardized Difference (Impella-IABP)	p Value
Age, years	69.2±10.9	71.4±10.9	-0.20	<0.0001
Male sex	65.6%	73.3%	-0.17	0.0003
Marital status				
Married	59.8%	51.7%	0.24	<0.0001
Single	28.1%	39.2%		
Other/unknown	12.1%	9.1%		
Patient race				
Black	6.6%	6.2%	0.16	0.022
Hispanic	4.0%	5.0%		
White	74.6%	69.1%		
Other	12.1%	17.3%		
Unknown	2.7%	2.4%		
Insurance payor				
Medicare	68.4%	73.0%	0.15	0.012
Medicaid	6.1%	7.5%		
Managed care/commercial	20.0%	15.8%		
Self-pay/other	5.5%	3.8%		
Admission type				
Elective	64.9%	79.8%	0.35	<0.0001
Urgent	34.1%	19.2%		
Trauma center	0.0%	0.1%		
N/A	1.0%	0.9%		
Hospital region				
South	32.2%	40.9%	0.25	<0.0001
Northeast	31.0%	22.2%		
Midwest	24.1%	21.3%		
West	12.7%	15.6%		
Hospital location				
Urban	92.4%	92.5%	-0.0031	0.93
Rural	7.6%	7.5%		
Teaching hospital	61.5%	60.2%	0.027	0.57
Total number of hospital beds				
0-99	1.1%	1.1%	0.17	0.024
100-199	3.1%	6.2%		
200-299	9.9%	7.8%		
300-399	18.6%	16.7%		
400-499	13.7%	15.3%		
500+	53.6%	52.9%		
High-cost co-morbidities				
Diabetes	40.5%	41.6%	-0.023	0.64
Congestive heart failure	34.1%	60.9%	-0.56	<0.0001
COPD	16.9%	17.1%	-0.0057	0.95
Chronic renal failure	6.9%	5.9%	0.042	0.34
Hypertension (any)	88.3%	88.1%	0.0056	0.94
Hypertension (essential)	44.9%	29.8%	0.32	<0.0001
Hypertension (non-essential)*	44.2%	59.2%	-0.31	<0.0001
Smoking†	15.0%	13.1%	0.054	0.23
Obesity‡	20.2%	13.6%	0.18	0.0001
Acute respiratory failure	7.6%	3.8%	0.165	0.0002
NSTEMI	32.6%	14.1%	0.45	<0.0001
PCI characteristics				
Multivessel PCI	29.2%	57.2%	0.59	<0.0001
Single-vessel PCI	70.8%	42.9%		
Other procedures				
Right heart catheterization	3.2%	4.4%	-0.061	0.20
Rotational atherectomy	4.8%	7.1%	-0.098	0.039
Intravascular ultrasound	17.2%	25.2%	-0.20	<0.0001
Transradial access	12.4%	10.6%	0.058	0.22
Bifurcation lesion§	0.6%	0.2%	0.058	0.23
Chronic coronary total occlusion	14.3%	21.7%	-0.20	<0.0001
Mechanical ventilation	20.2%	8.2%	0.35	<0.0001

(*continued*)

Table 1 (***Continued***)

Variable	IABP n = 709	Impella n = 1,447	Standardized Difference (Impella-IABP)	p Value
Medications				
Glycoprotein IIb/IIIa inhibitor	26.4%	6.5%	0.56	<0.0001
Ticagrelor	37.4%	36.8%	0.011	0.81
Prasugrel	6.4%	5.6%	0.032	0.49
Novel oral anticoagulant	7.2%	7.3%	-0.0024	1.00
Warfarin	6.4%	3.3%	0.15	0.001

COPD = chronic obstructive pulmonary disease; IABP = intra-aortic balloon pump; NSTEMI = non−ST−segment elevation myocardial infarction; PCI = percutaneous coronary intervention.

Values are mean ± SD or %. Standardized mean differences were estimated before and after propensity score adjustment.

*Nonessential hypertension includes hypertension with heart disease, hypertension with chronic kidney disease, and secondary hypertension diagnoses.

† Smoking includes nicotine dependence, uncomplicated or with withdrawal or in remission (codes in Supplementary Appendix 3).

‡ Obesity includes obesity, severe obesity, and overweight (codes in Supplementary Appendix 3).

§ Reported bifurcation lesions exclude left main interventions.

STEMI and the second, removing both STEMI and cardiogenic shock. The intent of these sensitivity analyses was to evaluate outcomes by treatment group by eliminating STEMI and/or cardiogenic shock as potential major confounders if miscoded as postprocedure complications rather than diagnoses present on admission (both exclusion criteria for our high-risk PCI population).

To assess predictors of in-hospital mortality, we performed a multivariable logistic regression analysis that included patient characteristics, outcomes, and treatment group in the propensity-adjusted population.

The sponsor of the study had no role in data collection, data analysis, data interpretation, writing the manuscript, or the decision to submit the manuscript. The authors had full access to all the data in the study and all co-authors reviewed the manuscript and provided input, vouched for the accuracy of the data, and agreed to submit the manuscript for publication.

Results

From April 2016 to June 2019, a total of 48,179 patients were treated with Impella or IABP MCS at 304 hospitals in the United States; among these, we identified 2,156 patients undergoing nonemergent high-risk PCI, including 1,447 patients (67.1%) treated with Impella and 709 patients (32.9%) treated with IABP (Supplementary Figure 1). Baseline demographics and clinical characteristics (codes included in Supplementary Appendix 3) are presented in Table 1. Before adjustment, Impella patients were older, more likely to be male, with Medicare insurance, had more congestive heart failure, multivessel PCI, and chronic coronary total occlusion than patients with IABP. Patients with IABP were more obese, had more acute respiratory failure, NSTEMI at presentation, single-vessel PCI, and glycoprotein IIb/IIIa inhibitor and warfarin use (Table 1). Standardized mean differences estimated before and after propensity adjustment, along with distributions of the propensity scores are presented in Supplementary Figure 2. Differences between treatments were controlled after propensity

Table 2
Unadjusted and adjusted in-hospital clinical outcomes: Impella versus IABP

Clinical Outcomes	Unadjusted				Adjusted	
	IABP n = 709	Impella n = 1,447	Odds Ratio (95% CI)	p Value	Odds Ratio (95% CI)	p Value
Survival	91.0%	95.3%	2.01 (1.41, 2.87)	0.0002	1.55 (1.02, 2.36)	0.042
Myocardial infarction	11.9%	2.5%	0.19 (0.13, 0.28)	<0.0001	0.29 (0.18, 0.46)	<0.0001
STEMI	8.2%	1.4%	0.16 (0.09, 0.26)	<0.0001	0.28 (0.15, 0.50)	<0.0001
NSTEMI	5.4%	1.3%	0.23 (0.12, 0.43)	<0.0001	0.33 (0.16, 0.72)	0.0500
Cardiogenic shock	18.9%	8.3%	0.39 (0.30, 0.51)	<0.0001	0.54 (0.39, 0.74)	0.0001
Stroke	2.3%	1.7%	0.73 (0.39, 1.38)	0.40	0.98 (0.46, 2.11)	0.96
Bleeding requiring transfusion	2.3%	2.5%	1.11 (0.61, 2.01)	0.88	1.18 (0.59, 2.37)	0.65
Acute kidney injury	1.6%	1.6%	1.02 (0.50, 2.11)	1.00	0.89 (0.39, 2.05)	0.78

IABP = intra-aortic balloon pump; MI = myocardial infarction; NSTEMI = non−ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

Unadjusted outcomes were assessed using chi-square or Fisher's exact tests and presented using odds ratios and 95% CIs. Adjusted outcomes were assessed using multivariable logistic regression. Doubly robust models adjusted for the propensity score estimates as well as additional selected baseline covariates present on admission. The resulting adjusted odds ratios along with 95% CI are presented. The significance threshold was set at an alpha <0.05 without adjustment for multiplicity.

Table 3
Sensitivity analyses of in-hospital clinical outcomes

1. Removing STEMI

Clinical Outcomes	Unadjusted				Adjusted	
	IABP n = 651	Impella n = 1,427	Odds Ratio(95% CI)	p Value	Odds Ratio(95% CI)	p Value
Survival	92.0%	95.9%	2.05 (1.39, 3.02)	0.0003	1.49 (0.94, 2.36)	0.090
NSTEMI	6.1%	1.3%	0.20 (1.08, 0.38)	<0.0001	0.31 (0.15, 0.67)	0.0028
Cardiogenic shock	16.4%	7.5%	0.41 (0.31, 0.55)	<0.0001	0.53 (0.38, 0.75)	0.0003
Stroke	2.0%	1.7%	0.84 (0.43, 1.66)	0.61	1.22 (0.54, 2.76)	0.63
Bleeding requiring transfusion	2.0%	2.3%	1.16 (0.61, 2.22)	0.65	1.21 (0.57, 2.56)	0.62
Acute kidney injury	1.7%	1.5%	0.91 (0.44, 1.89)	0.80	0.84 (0.36, 1.94)	0.68

2. Removing STEMI or Cardiogenic Shock

Clinical Outcomes	Unadjusted				Adjusted	
	IABPn = 544	Impella n = 1,320	Odds Ratio(95% CI)	p Value	Odds Ratio(95% CI)	p Value
Survival	94.3%	98.4%	3.74 (2.13, 6.57)	<0.0001	3.21 (1.62, 6.36)	0.0009
NSTEMI	5.3%	0.6%	0.11 (0.05, 0.27)	<0.0001	0.17 (0.06, 0.48)	0.0010
Stroke	1.7%	1.3%	0.78 (0.34, 1.75)	0.54	0.94 (0.34, 2.59)	0.91
Bleeding requiring transfusion	1.8%	1.3%	0.70 (0.32, 1.53)	0.37	0.96 (0.36, 2.51)	0.93
Acute kidney injury	1.5%	1.4%	0.93 (0.40, 2.14)	0.86	0.89 (0.33, 2.37)	0.81

Statistical analyses were performed as presented in Table 2. Abbreviations as in Table 2.

adjustment. The c-statistic for the propensity model was 0.824, indicating excellent discriminatory ability.

The unadjusted in-hospital survival rate was significantly higher with Impella than the IABP (95.3% vs 91.0%; OR 2.01, 95% CI 1.41 to 2.87) (Table 2). Unadjusted rates of subsequent MI and cardiogenic shock were significantly lower with Impella than the IABP (Table 2). There were no significant differences between groups in the rates of stroke, bleeding, or AKI. After adjustment, patients with Impella had improved survival (OR 1.55, 95% CI 1.02 to 2.36) and lower rates of MI (OR 0.29, 95% CI 0.18 to 0.46) and cardiogenic shock (OR 0.54, 95% CI 0.39 to 0.74) than IABP (Table 2). There were no differences in the adjusted odds of stroke, bleeding requiring transfusion, or AKI between the treatment groups; however, the odds of experiencing AKI in the Impella group was lower after risk adjustment than the unadjusted model (0.89 vs 1.02) (Table 2).

The first sensitivity analysis removed patients with STEMI for possible miscoding as being absent on admission (Supplementary Figure 3). Results remained consistent with greater unadjusted survival rate with Impella than with IABP (95.9% vs 92.0%, p = 0.0003), as well as improved rates of NSTEMI and cardiogenic shock (p <0.0001) (Table 3). There were no differences in stroke, bleeding, or AKI between groups. After adjustment, the survival benefit was no longer significant with Impella (OR 1.49, 95% CI 0.94 to 2.36, p = 0.090), whereas the benefit in reducing NSTEMI and cardiogenic shock rates remained significant (Table 3).

We performed a second sensitivity analysis that removed patients with STEMI or cardiogenic shock as possibly miscoded as a complication rather than present on admission (Supplementary Figure 3). Results remained consistent, favoring greater survival (unadjusted rates: 98.4% vs 94.3%; adjusted OR 3.21, 95% CI 1.62 to 6.36) and less NSTEMI (unadjusted rates: 0.6% vs 5.3%; adjusted OR 0.17, 95% CI 0.06 to 0.48) in the Impella group (Table 3). There were no significant differences in the rates of stroke, bleeding, or AKI between groups.

Hospital LOS was significantly shorter by approximately 2.4 days with Impella in the unadjusted population (3.1 days with Impella vs 5.5 days with IABP), a difference that was attenuated to approximately 1.4 days but remained significant after adjustment (3.4 days with Impella vs 4.8 days with IABP). Overall, the average unadjusted index hospitalization costs with Impella were 27% higher than with IABP and 37% higher in the adjusted population (Table 4). For surviving patients, Impella costs were 43% higher ($47,541 with Impella vs $33,240 IABP, p <0.0001) in the adjusted population. LOS and index hospital costs were consistent in both sensitivity analyses (Supplementary Table 1).

Univariate analyses are presented in Supplementary Table 2. Multivariable logistic regression of the primary propensity-adjusted population identified the following in-hospital complications as predictors of in-hospital mortality: MI, cardiogenic shock, stroke, and bleeding requiring transfusion. Developing cardiogenic shock after PCI was the strongest predictor of in-hospital mortality (OR 7.54, 95% CI 4.97 to 11.45) (Figure 1).

Discussion

This propensity-adjusted, population-based analysis of patients undergoing nonemergent MCS supported high-risk PCI suggests that Impella support is associated with a 55% improvement in survival, a 71% reduction in MI, and a 46% reduction in cardiogenic shock, with no observed difference in the rate of stroke, bleeding requiring transfusion, or AKI. Sensitivity analyses designed to evaluate the robustness of the data and eliminate major confounding from possible coding errors largely mirrored the trends observed in the overall population. Patients treated with Impella-supported high-risk PCI had better in-hospital

Table 4
Unadjusted and adjusted economic outcomes: Impella versus IABP

Economic Outcomes	Unadjusted				Adjusted			
	IABP n = 709	Impella n = 1,447	Difference (%)	p Value	IABP n = 709	Impella n = 1,447	Difference (%)	p Value
LOS/Costs (All Patients)					**LOS/Costs (All Patients)**			
Index LOS, mean	5.5	3.1	-44.34%	<0.0001	4.8	3.4	-29.11%	<0.0001
Index LOS, median (Q1, Q3)	4.0 (2.0, 7.0)	2.0 (1.0, 3.0)			4.8 (4.6, 5.0)	3.4 (3.3, 3.5)		
Index costs, mean	$37,625	$47,819	27.10%	<0.0001	$35,655	$48,784	36.82%	<0.0001
Index costs, standard deviation	$32,230	$28,795	-10.66%	—	$32,267	$28,801	-10.74%	—
LOS/Costs (Surviving Patients)					**LOS/Costs Surviving Patients)**			
Index LOS, mean	5.3	3.0	-43.59%	<0.0001	4.5	3.3	-25.77%	<0.0001
Index LOS, median (Q1, Q3)	4.0 (2.0, 7.0)	1.0 (1.0, 3.0)			4.4 (4.3, 4.7)	3.3 (3.2, 3.4)		
Index costs, mean	$34,889	$46,770	34.05%	<0.0001	$33,240	$47,541	43.02%	<0.0001
Index costs, standard deviation	$25,620	$27,751	8.32%	—	$25,340	$27,721	9.40%	—

LOS = length of stay (day).
Unadjusted outcomes were assessed using independent-sample *t* tests. Adjusted outcomes were analyzed using linear regression model.

survival and outcomes and shorter LOS at the expense of higher average index hospital costs compared with IABP. Developing cardiogenic shock after PCI was the strongest predictor of in-hospital mortality.

The benefits of stabilizing hemodynamics with MCS devices during "high-risk" PCI are to prevent hemodynamic collapse, enable optimal revascularization, and improve clinical outcomes. The PROTECT II trial demonstrated a reduction in the rates of death, stroke, MI, or the composite of death/stroke/MI at 90 days with Impella 2.5 compared with IABP among patients who received the intended MCS device (per protocol).[4] In a post hoc multivariable analysis, Impella use was an independent predictor of freedom from major adverse events (OR 0.75, 95% CI 0.61 to 0.92) and major adverse cardiac and cerebral events (OR 0.76, 95% CI 0.61 to 0.96) at 90 days after the procedure.[16] These benefits extended to patients achieving complete revascularization.[17] Our findings in a contemporary "real-world" population are consistent with and extend the PROTECT II trial results.

Our results, however, contrast recently published large-scale studies of Impella use for broad indications, including STEMI, cardiogenic shock, and high-risk PCI, and in acute MI that reported worse in-hospital outcomes with Impella

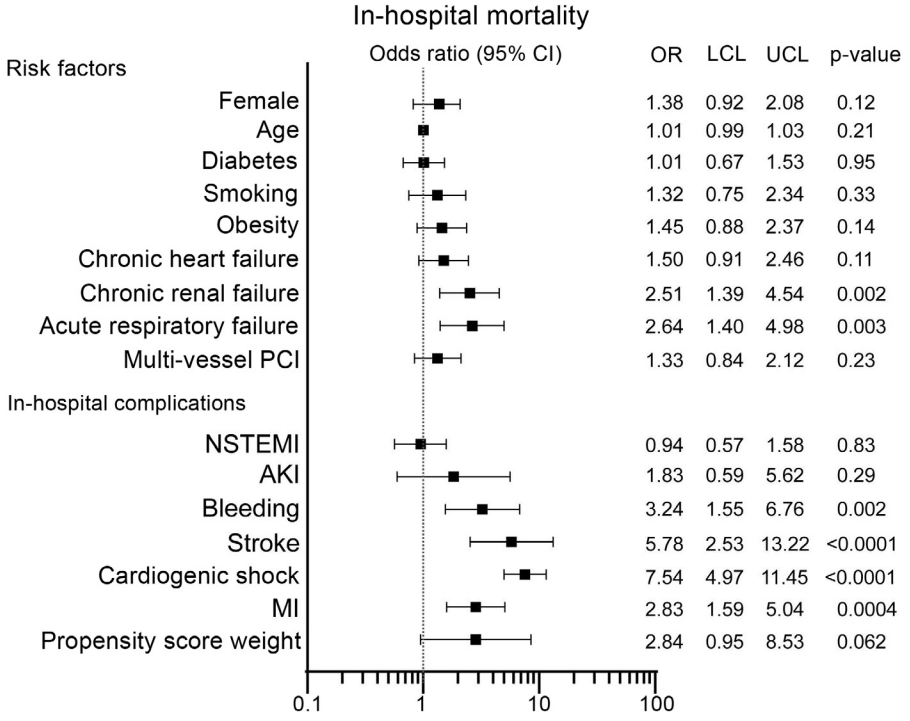

Figure 1. Predictors of in-hospital mortality. Forest plot of multivariable logistic regression analysis of the propensity-adjusted population demonstrating the contribution of in-hospital complications to mortality. Patient characteristics are on admission. For age, the OR corresponds to a 1-year increase in patient age. LCL = lower confidence limit; UCL = upper confidence limit.

than IABP.[11,12] Notable differences in reported outcomes of the previous study using the same PHD maybe due to (1) the undifferentiated population studied, (2) inclusion of patients from a time period that preceded Impella approval (2004 to 2016), impacting patient complexity, and (3) confounding resulting from the broad spectrum of clinical presentations included in the study population.[11] In contrast, our aim was to use the PHD to represent real-world practice focused on a single clinical indication (high-risk PCI), in a timeframe limited to Food and Drug Administration-approved indication of Impella, using propensity-adjusted methodology and sensitivity analyses to address confounders and possible inherent miscoding of claims data. In this more narrowly defined context, our results suggest the benefit of Impella use compared with IABP for high-risk PCI indication.

Potential mechanisms of the benefit of Impella are the reduction of in-hospital cardiogenic shock with Impella compared with IABP, which was the strongest identified predictor of mortality in our study. In addition, our analysis did not identify an increased risk of stroke or bleeding requiring transfusion with Impella compared with IABP. Our data align with a recent meta-analysis, showing no added bleeding risk with percutaneous ventricular assist devices compared with IABP.[18] Improvements in bleeding rates in our study are consistent with recent series of large-bore access devices, where ultrasound-guided access techniques have become the norm in contemporary practice (as seen in transcatheter aortic valve replacement), reducing vascular complications. These findings are relevant due to the strong contribution of stroke and bleeding to in-hospital mortality, with stroke conferring an approximately 6-fold mortality risk and bleeding an approximately 3-fold higher mortality risk based on our study. Therefore, careful re-evaluation of contemporary interventional practice, including use of large-bore MCS, is warranted with the rapid evolution of clinical practice and interventional techniques.

Although Impella use reduced index LOS, index hospitalization costs remained higher with Impella, as was previously shown using PHD[11] and in the PROTECT II cost-effectiveness study ($47,667 with Impella vs $33,684 with IABP, $p < 0.001$).[19] However, because readmission LOS and costs were lower for Impella, after 90 days, the total hospital charges were similar for Impella and IABP ($172,564 vs $172,758, respectively, $p = 0.785$), suggesting that the initial cost differential may be offset at 90 days, based on improved readmission LOS and less use of critical care admissions.[19]

Our study should be interpreted in the context of the inherent limitations of large claims datasets designed for the purpose of billing rather than for assessing comparative effectiveness of treatment strategies and the selection criteria for the population. The selection criteria for "high-risk PCI" and the decision to use MCS and the type were determined by the treating physician, limiting our ability to specifically define the criteria for high-risk PCI. Other inherent limitations include coding inconsistencies across providers, lack of detailed diagnosis, timing, and indication for Impella/IABP use (planned or bailout), potential access site or aortoiliac disease, coronary or peripheral disease severity characterization, hemodynamic data, or frailty, and limited physiologic measurement and other relevant information, many of which can contribute to possible bias in the selection of IABP versus Impella and unmeasured confounding. We limited our population to those undergoing single-PCI procedures to exclude PCI complications during the same admission; this unavoidably excluded some (but not all) high-risk patients with left main or multivessel disease treatment that were staged during the same hospitalization. The matching process against a benchmark of high-risk patients treated with Impella resulted in a selective and smaller sample of patients treated with IABP. Although the present study featured rigorous methods and doubly robust analyses to lessen the impact of these limitations, these do not eliminate the potential for remaining unmeasured confounders; therefore, this study should be interpreted in the context of these inherent limitations.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.08.032.

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