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ORIGINAL RESEARCH

Percutaneous Microaxial Ventricular Assist Device Versus Intra-Aortic Balloon Pump for Nonacute Myocardial Infarction Cardiogenic Shock

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BACKGROUND: Evidence on the comparative outcomes following percutaneous microaxial ventricular assist devices (pVAD) versus intra-aortic balloon pump for nonacute myocardial infarction cardiogenic shock is limited.

METHODS AND RESULTS: We included 704 and 2140 Medicare fee-for-service beneficiaries aged 65 to 99 years treated with pVAD and intra-aortic balloon pump, respectively, for nonacute myocardial infarction cardiogenic shock from 2016 to 2020. Patients treated using pVAD compared with those treated using intra-aortic balloon pump were more likely to be concurrently treated with mechanical ventilation, renal replacement therapy, and blood transfusions. We computed propensity scores for undergoing pVAD using patient- and hospital-level factors and performed a matching weight analysis. The use of pVAD was associated with higher 30-day mortality (adjusted odds ratio, 1.92 [95% CI, 1.59–2.33]) but not associated with in-hospital bleeding (adjusted odds ratio, 1.00 [95% CI, 0.81–1.24]), stroke (adjusted odds ratio, 0.91 [95% CI, 0.56–1.47]), sepsis (OR, 0.91 [95% CI, 0.64–1.28]), and length of hospital stay (adjusted mean difference, +0.4 days [95% CI, –1.4 to +2.3]). A quasi-experimental instrumental variable analysis using the cross-sectional institutional practice preferences showed similar patterns, though not statistically significant (adjusted odds ratio, 1.38; 95% CI, 0.28–6.89).

CONCLUSIONS: Our investigation using the national sample of Medicare beneficiaries showed that the use of pVAD compared with intra-aortic balloon pump was associated with higher mortality in patients with nonacute myocardial infarction cardiogenic shock. Providers should be cautious about the use of pVAD for nonacute myocardial infarction cardiogenic shock, while adequately powered high-quality randomized controlled trials are warranted to determine the clinical effects of pVAD.

Key Words: cardiogenic shock ■ endovascular procedures ■ heart-assist device ■ mechanical circulatory support ■ Medicare

Cardiogenic shock (CS) is a critical condition associated with high morbidity and mortality worldwide.[1,2] Despite the technological advancements in medicine, including the development of various mechanical circulatory support (MCS) devices, mortality has not been improving at ≈30% to 50% over the past 20 years.[2,3] Since the United States Food and Drug Administration approved a percutaneous microaxial ventricular assist device (pVAD) following a randomized controlled trial (RCT) showing improved hemodynamic

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CLINICAL PERSPECTIVE

What Is New?

- Using the Medicare database, we implemented several analytical approaches, such as propensity score matching weight and instrumental variable analysis and showed that the use of a percutaneous microaxial ventricular assist device was associated with higher mortality compared with intra-aortic balloon pump in patients with nonacute myocardial infarction cardiogenic shock.

What Are the Clinical Implications?

- Because causal inferences using administrative databases may be challenging, adequately powered high-quality randomized clinical trials are needed to determine the clinical effects of percutaneous microaxial ventricular assist devices in nonacute myocardial infarction cardiogenic shock.

Nonstandard Abbreviations and Acronyms

CS	cardiogenic shock
IABP	intra-aortic balloon pump
IV	instrumental variable
MCS	mechanical circulatory support
MW	matching weight
PS	propensity score
pVAD	percutaneous microaxial ventricular assist device

parameters in patients undergoing high-risk percutaneous coronary intervention supported by pVAD compared with intra-aortic balloon pump (IABP),[4] the use of pVADs has been increasing in the United States, including for patients with CS.[5–7] However, given that the efficacy and effectiveness of pVAD for CS have not been rigorously tested, concerns have been raised about the appropriateness of using pVAD for CS.[8] Indeed, several RCTs have failed to show the survival benefits of pVAD for CS.[9–12] However, it is challenging to conduct large-scale, high-quality RCTs due to the complex nature of the condition and the procedure. Therefore, comparative effectiveness research using observational data may add valuable insights.[5–7,13–16]

As for CS related to acute myocardial infarction (AMICS), a previous study using various causal inference methods showed inconsistent findings by different methodologies and emphasized the need for RCTs in this area.[14] However, due to the difference in the pathophysiology and clinical trajectories,[17,18] it remains unclear whether these findings would apply to the non-AMICS population. Furthermore, although some studies investigated the use of MCS devices for non-AMICS, they did not separate different MCS devices and did not examine the effectiveness of pVADs alone.[13,19]

To fill these important knowledge gaps, we conducted a retrospective observational study using the Medicare claims database. We aimed to evaluate the comparative effectiveness of pVAD to IABP in patients with non-AMICS with multiple statistical approaches.

METHODS

This study followed the STROBE (Strengthening the reporting of observational studies in epidemiology) guidelines.[20] The data that support the findings of this study are available from the corresponding author upon reasonable request. This study was reviewed by the University of California Los Angeles Institutional Review Board and granted an exemption with a waiver for patient consent given the nature of the secondary analysis of existing databases.

Data Source

We used the 100% sample Medicare fee-for-service Inpatient Claims and Beneficiary Summary files for the analyses of clinical outcomes and linked them with the 20% random sample Carrier File for the analysis of health care spending. These administrative databases compile all claims made by acute care hospitals for services provided to Medicare beneficiaries under the fee-for-service program. Patient information, such as unique beneficiary identifier, age, gender, race and ethnicity, diagnoses under *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes with a flag indicating whether the diagnosis was present on admission or not, discharge date, procedure codes under the *ICD-10*-procedure coding system and date the procedure was performed, and unique hospital identifier, are available. We linked the database of the American Hospital Association to obtain hospital-level covariates. Hospitals without linkage to the American Hospital Association database were excluded.

Patients

We used the 100% Medicare fee-for-service Inpatient Claims and Beneficiary Summary files to identify eligible patients. Patients were included if they were aged between 65 and 99 years and were admitted with a record of CS on admission for the first time between January 1, 2016, and November 30, 2020. Patients were excluded if they had a diagnosis of acute myocardial infarction on admission (determined by the

presence of corresponding *ICD-10* codes) or revascularization procedures (ie, percutaneous coronary intervention or coronary artery bypass grafting) on the day of or before the initiation of pVAD or IABP.[18,21] Patients with diagnoses of bleeding, stroke, and sepsis on admission were also excluded. Patients on extracorporeal membrane oxygenation on the day of or before the initiation of pVAD or IABP were also excluded because CS management and left ventricle unloading may carry clinically different implications.[22] We implemented an active comparator design with the day of the treatment initiation (pVAD versus IABP) as the cohort entry. We excluded patients who had undergone both pVAD and IABP throughout the hospitalizations.[7] *ICD-10* diagnosis and procedure codes used for data extraction are summarized in Table S1. When a patient was transferred to another acute care hospital, the claims made at the hospital after inter-hospital transfer were also included in the analyses to improve traceability. Inter-hospital transfers were identified when a patient was discharged from the index hospital with a status of "Discharged/transferred to another short-term general hospital for inpatient care" and admitted to another hospital on the same day of discharge from the index hospital.[23]

Covariates

We collected the following patient information: age in 5-year increments (65–69, 70–74, 75–79, 80–84, and ≥85 years), gender, race and ethnicity group (non-Hispanic White, non-Hispanic Black, Hispanic, or other [Unknown, Asian/Pacific Islander, American Indian/Alaska Native, and Other]), median household income of zip code (in 10ths), underlying comorbidities (ie, congestive heart failure, prior acute myocardial infarction, ischemic heart disease, atrial fibrillation [AF], hypertension, diabetes, chronic kidney disease, hyperlipidemia, peripheral vascular disease, prior stroke or transient ischemic attack, chronic obstructive pulmonary disease, anemia, cancer, depression, arthritis, liver disease, and Alzheimer dementia). We also extracted admission day (weekday or weekend), conditions on admission (ventricular tachycardia or ventricular fibrillation and cardiac arrest), and concomitant treatments on the day of or before the initiation of pVAD or IABP, including invasive mechanical ventilation (IMV), pulmonary artery catheter, vasopressors, renal replacement therapy, and blood transfusion.

Regarding hospital-level characteristics, we collected the annual case volume of CS, pVADs, VAD implantation, and heart transplant by averaging the number of cases in Medicare beneficiaries in each hospital over the study period. We also extracted the number of hospital beds and geographical location (urban versus nonurban) from the American Hospital Association database.

Outcomes

Our primary outcome was 30-day mortality from the initiation of pVAD or IABP. The secondary outcomes included in-hospital outcomes, such as bleeding,[7] stroke, sepsis,[24] length of hospital stay among survivors, and total health care spending during hospitalization. Events recorded after inter-hospital transfers were counted as in-hospital outcomes.

As we needed to include the data on health care spending available in the Medicare Carrier Files, we used a 20% sample for the analysis of health care spending. We defined the health care spending as the total of the Medicare payment (the amount Medicare paid for the services plus per diem amount multiplied by the utilization day counts), the primary payer payment, beneficiary liability for cost sharing (coinsurance, co-pays, and deductibles), and payment due to the providers.[25,26]

Statistical Analysis

We performed a propensity score (PS) matching weight (MW) analysis to compare the outcomes of patients treated with pVAD versus IABP.[27,28] First, we computed a PS for pVAD or IABP in each patient using a multivariable logistic regression model. As patient-level factors, we included age, gender, race and ethnicity, median household income of zip code, comorbidities, conditions on admission, admitted year, admission day (weekday or weekend), concomitant treatments on the day of or before the initiation of pVAD or IABP, and the day of the index procedures from hospital admission. Additionally, we included the institutional volumes of CS, pVAD, VAD implantation, and heart transplant, as well as bed number and geographical location to account for the variability in practice patterns across hospitals. C-statistics was calculated as the measure of the discriminability of PS. Second, we computed MW by dividing either PS for undergoing pVAD or IABP (whichever is smaller) by the PS for the assigned treatment (therefore, MW ranges from 0 to 1). As opposed to the conventional PS matching method, MW analysis does not exclude patients without pairs, thereby allowing more efficient estimation even when group sizes are not similar. Furthermore, as opposed to the conventional inverse probability of treatment weighting method (the weight of which can range from 1 to infinite), the target of inference focuses on patients who have a close propensity score (similar to PS matching), thereby allowing more stable estimation even when covariates are not similar.[29] The balances between the 2 groups were considered acceptable when standardized mean difference was 0.1 or lower.[30] The distribution of the propensity score before and after MW computation was visualized with the density plots. We applied logistic regression for binary outcomes and

linear regression for continuous outcomes, with each subject weighted by MW. Cumulative mortality was visualized by Kaplan–Meier plots. E-value was calculated to quantify the unmeasured confounding needed to nullify the statistical significance for mortality.[31] For the assessment of health care spending, because Medicare payments vary with geographical regions, we included hospital as a fixed effect in the regression model to sufficiently account for the geographical variability of the Medicare payment.

To explore specific population associated with the effectiveness or safety related to the use of pVAD, we performed subgroup analyses according to the patient age (<75 versus ≥75), underlying congestive heart failure, underlying ischemic heart disease, cardiac arrest on admission, concomitant IMV, institutional case volume quartiles of pVAD (Q1 versus Q2 versus Q3 versus Q4 for patient number), and admission year (2016–2018 versus 2019–2020). PS was recalculated for each subgroup.

We performed several sensitivity analyses. First, we conducted a conventional PS matching analysis using the 1:1 nearest-neighbor method without replacement. A match occurred when a patient in the pVAD group had an estimated propensity score within 0.2 SDs of a patient in the IABP group. The exact-match method was applied for the day of the index procedures, ensuring that matched patients received either pVAD or IABP on the same hospital day. Second, to effectively compare the outcomes of patients treated with pVAD versus IABP within the same hospital and to account for missing values in income, we performed multivariable logistic regression analyses with hospital fixed effect, weighted by the inverse probability of the income information being observed.[32,33] Third, we performed MW analysis, restricting the patients to those who received pVAD or IABP on the day of admission or the next day (hospital day 0 or 1) and excluded those discharged (either dead or alive) on hospital day 0 or 1 to avoid an immortal time bias.[34] Fourth, to investigate whether our findings were sensitive to the outcome definitions, we used 60-day mortality instead of 30-day mortality and blood transfusion after the treatment initiation instead of *ICD-10* codes-defined bleeding.[33] Those treated after October 31, 2020 were excluded from 60-day mortality analysis. Fifth, to overcome potential unmeasured confounding, we performed an instrumental variable (IV) analysis.[14] We calculated the percentage of pVAD use among all pVAD or IABP use for non-AMICS from 1 year before each index procedure at a given institution and treated the percentage as the instrument (therefore, patients who received pVAD or IABP before January 1, 2017, were excluded), assuming that an institution's prior use of pVAD was a strong predictor of the probability of using the device for subsequent hospitalizations. We used a 2-stage residual inclusion approach using the "ivtools" package.[35] In the first stage, we developed a multivariable logistic regression model to predict the use of pVAD as a function of the instrumental variable and the patient- and hospital-level characteristics. F-statistics was calculated to evaluate the relevance assumption, with the cut-off being 10.[36] In the second stage, we used a logistic regression model in which an outcome was treated as a dependent variable, including the residuals from the first-stage model, as well as the patient and hospital-level variables as independent variables.[36] To indirectly assess the exclusion restriction and exchangeability assumptions of the IV, we divided the cohort into 3 groups according to the tertile of the instrument and evaluated standardized mean differences of patient and hospital-level characteristics.

Data preparation was conducted using SAS, version 9.4 (SAS Institute Inc, Cary, NC), and analyses were performed using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Cohort

We included 2844 patients meeting our selection criteria in our analyses, of which 704 and 2140 patients were treated with pVADs and IABP, respectively (Figure 1). Patient-level and hospital-level characteristics are summarized in Table 1. In brief, the median age was 72 years (interquartile range, 68–77), 30.2% (n=860) were women, and 6.9% (n=195) had cardiac arrest on admission. Patients treated with pVADs were more likely than those treated with IABP to have received IMV, renal replacement therapy, and blood transfusion as concomitant treatments. As hospital-level characteristics, the median case volume of pVADs was higher in the pVAD group, while that of CS and VAD implantation was higher in the IABP group. The median hospital day of the index procedures was 1 day (interquartile range, 0–2) for pVADs and 0 day (interquartile range, 0–3) for IABP (Figure S1).

Principal Analysis

In the unadjusted cohort, patients treated with pVAD had higher 30-day mortality than those treated with IABP (55.4% [390/704] versus 35.6% [762/2140]; odds ratio [OR], 2.25; 95% confidence interval [CI], 1.89– 2.67). Length of hospital stay among survivors and health care spending in each group were visualized in Figures S2 and S3. In the MW analysis, the measured patient-level and hospital-level characteristics were well-balanced between the 2 groups. The C-statistics of the PS was 0.74. The distribution of the PS is shown in Figure S4. The use of pVAD was associated with higher 30-day mortality than IABP (55.0%

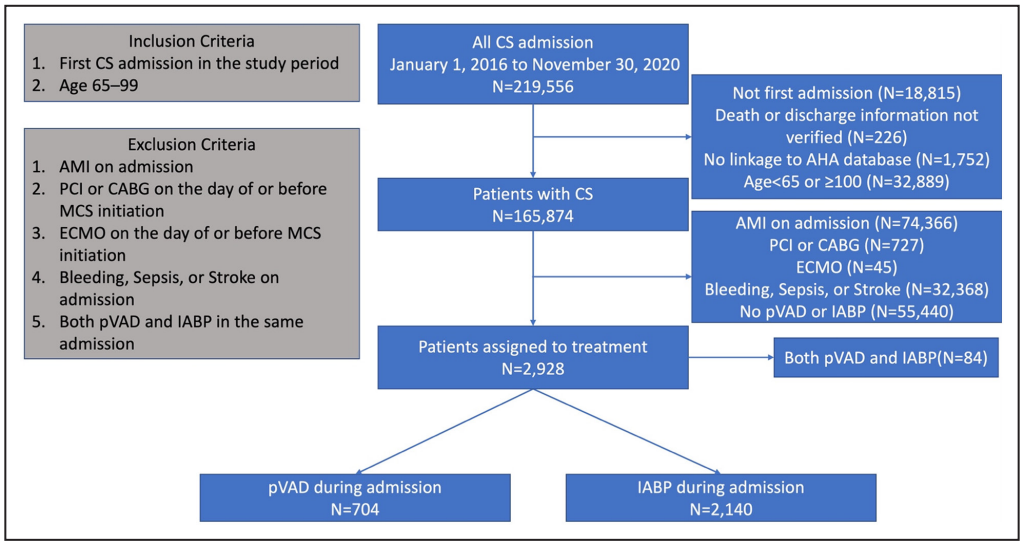

Figure 1. Flowchart of patient selection.
AHA indicates American Hospital Association; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support (= pVAD or IABP); pVAD, percutaneous microaxial ventricular assist device; and PCI, percutaneous coronary intervention.

[355/645] versus 38.9% [248/639]; adjusted odds ratio [aOR], 1.92; 95% CI, 1.59– 2.33; Figure S5) but not associated with bleeding, stroke, sepsis, LOS among survivors, and health care spending (Table 2). The E-value for 30-day mortality was 2.12 with a lower bound of 1.83.

Subgroup Analyses

Subgroup analyses showed qualitatively similar results to the principal analysis. The point estimates of odds ratios for 30-day mortality were >1 for pVAD compared with IABP in all subgroups (Figure 2). The other studied outcomes mostly showed similar results to the principal analysis, although the use of pVAD was associated with higher health care spending in some subgroups (Figures S6–S10).

Sensitivity Analyses

A series of sensitivity analyses, including the PS matching analysis, multivariable logistic regression with hospital fixed effect, and MW analysis with patients undergoing pVAD or IABP on hospital days 0–1, showed qualitatively consistent results (Figure 3; Tables S2–S4). These findings remained similar when 60-day mortality was used instead of 30-day mortality (58.7% [373/635] versus 42.5% [268/630]; adjusted odds ratio, 1.92 [95% CI, 1.58–2.33]) or blood transfusion was used instead of *ICD-10*-defined bleeding (7.0% [45/645] versus 7.0% [45/640]; adjusted odds ratio, 1.01 [95% CI, 0.70–1.46]).

For IV analysis, the percentage of pVAD use among non-AMICS patients in a given institution ranged from 0% to 100% with a skewed distribution (Figure S11). The F-statistic of the instrument was 35.6, indicating that the previous institutional practice pattern was a strong predictor of the use of pVAD. Several variables were not well balanced across groups defined by the level of pVAD use, such as concomitant use of IMV, pulmonary artery catheter, and institutional volumes of CS and heart transplant (Table S5). We found a similar pattern for 30-day mortality, although statistical significance was not achieved (Figure 3).

DISCUSSION

Our investigation of non-AMICS using a nationally representative database revealed several important findings: (1) all analyses using measured confounding variables consistently showed higher mortality in patients undergoing pVAD than those treated with IABP; (2) however, the higher mortality with the use of pVAD was attenuated in the IV analysis; (3) no evidence was observed in the risk of in-hospital complications between the use of pVAD and IABP in non-AMICS; (4) the use of pVAD may be associated with higher health care spending in some settings.

Examining the clinical effectiveness of MCS devices is challenging because of the sample size issue of RCTs and unmeasured confounding in observational studies. Although several RCTs have been attempted,[9–11] their power to detect the differences in hard end points may be limited by the small sample sizes ranging from 12 to 48 patients in each study. There are larger RCTs currently ongoing, including

Table 1. Patient-Level and Hospital-Level Characteristics in the Unadjusted Cohort and Matching Weight Analysis

	Unadjusted cohort			Matching weight analysis		
	pVAD (N=704)	IABP (N=2140)	SMD	pVAD (N=645)	IABP (N=640)	SMD
Baseline characteristics						
Age	72.0 (68.0–76.3)	72.0 (68.0–77.0)	0.041	72.0 (68.0–77.0)	72.0 (68.0–77.0)	0.008
Women	201 (28.6)	659 (30.8)	0.049	184 (28.5)	182 (28.5)	0.001
Race and ethnicity			0.076			0.010
Non-Hispanic White	557 (79.1)	1663 (77.7)		511 (79.2)	507 (79.4)	
Non-Hispanic Black	77 (10.9)	236 (11.0)		70 (10.8)	69 (10.8)	
Hispanic	31 (4.4)	130 (6.1)		29 (4.6)	28 (4.3)	
Other*	39 (5.5)	111 (5.2)		35 (5.4)	35 (5.5)	
Median household income	62630 (49 377–79106)	63036 (50 493–82029)	0.019	62632 (49 424–78877)	62771 (49 956–80202)	0.021
Income information unavailable	18 (2.6)	52 (2.4)	0.008	0	0	<0.001
Underlying comorbidities						
CHF	482 (68.5)	1494 (69.8)	0.029	442 (68.5)	447 (69.9)	0.031
Prior AMI	27 (3.8)	102 (4.8)	0.046	25 (3.9)	24 (3.7)	0.010
Ischemic heart disease	494 (70.2)	1574 (73.6)	0.075	456 (70.7)	454 (71.0)	0.006
Atrial fibrillation	182 (25.9)	575 (26.9)	0.023	166 (25.7)	167 (26.2)	0.012
Hypertension	539 (76.6)	1653 (77.2)	0.016	496 (76.9)	492 (77.0)	0.002
Diabetes	311 (44.2)	911 (42.6)	0.032	286 (44.3)	284 (44.3)	0.001
CKD	390 (55.4)	1223 (57.1)	0.035	358 (55.6)	360 (56.3)	0.014
Hyperlipidemia	452 (64.2)	1355 (63.3)	0.018	415 (64.4)	414 (64.7)	0.006
Peripheral vascular disease	141 (20.0)	457 (21.4)	0.033	132 (20.5)	135 (21.1)	0.013
Stroke or TIA	32 (4.5)	98 (4.6)	0.002	30 (4.7)	30 (4.7)	<0.001
COPD	144 (20.5)	455 (21.3)	0.020	132 (20.4)	131 (20.6)	0.003
Anemia	285 (40.5)	903 (42.2)	0.035	264 (40.9)	264 (41.3)	0.008
Obesity	181 (25.7)	467 (21.8)	0.091	161 (24.9)	159 (24.9)	0.001
Cancer	82 (11.6)	218 (10.2)	0.047	78 (12.0)	79 (12.4)	0.012
Depression	98 (13.9)	344 (16.1)	0.060	91 (14.1)	95 (14.9)	0.023
Arthritis	197 (28.0)	604 (28.2)	0.005	184 (28.6)	178 (27.9)	0.015
Liver disease	83 (11.8)	248 (11.6)	0.006	76 (11.7)	76 (11.9)	0.004
Alzheimer dementia	41 (5.8)	163 (7.6)	0.072	39 (6.1)	41 (6.5)	0.016
Admission status and concomitant treatments on the day of or before the initiation of MCS						
Weekend admission	141 (20.0)	401 (18.7)	0.033	125 (19.4)	122 (19.1)	0.006
VT or VF	276 (39.2)	647 (30.2)	0.189	246 (38.1)	245 (38.4)	0.004
CA	58 (8.2)	137 (6.4)	0.071	52 (8.1)	50 (7.8)	0.011
IMV	386 (54.8)	839 (39.2)	0.317	346 (53.7)	342 (53.4)	0.005
PAC	139 (19.7)	408 (19.1)	0.017	127 (19.7)	127 (19.9)	0.004
Vasopressors	128 (18.2)	338 (15.8)	0.064	116 (18.0)	117 (18.3)	0.008
RRT	37 (5.3)	47 (2.2)	0.162	28 (4.4)	29 (4.6)	0.010
Transfusion	53 (7.5)	61 (2.9)	0.212	37 (5.7)	37 (5.9)	0.005
Hospital day MCS was initiated	1.0 (0.0–2.0)	0.0 (0.0–3.0)	0.083	1.0 (0.0–2.0)	0.0 (0.0–2.0)	0.008
Hospital characteristics						
Bed number	516 (320–747)	603 (345–861)	0.170	512 (320–742)	509 (307–747)	0.020
Annual volume of CS	85.3 (46.0–136.5)	107.2 (48.0–193.4)	0.318	84.8 (45.8–136.2)	89.0 (45.2–145.6)	0.027
Annual volume of pVAD	12.7 (6.8–19.8)	9.8 (4.2–17.0)	0.252	12.4 (6.6–19.2)	11.6 (4.4–21.4)	0.015
Annual volume of VAD	0.8 (0.0–9.0)	4.8 (0.0–13.8)	0.400	0.8 (0.0–9.3)	1.0 (0.0–10.2)	0.019
Annual volume of heart transplant	0.0 (0.0–4.0)	0.0 (0.0–8.6)	0.303	0.0 (0.0–4.0)	0.0 (0.0–5.8)	0.015
Urban	688 (97.7)	2082 (97.3)	0.028	630 (97.7)	620. (97.0)	0.044

Values are n (%) or median (25th–75th percentile).

Matching weight was performed with complete case analysis.

AMI indicates acute myocardial infarction; CA, cardiac arrest; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CS, cardiogenic shock; IABP, intra-aortic balloon pump; IMV, invasive mechanical ventilation; MCS, mechanical circulatory support; PAC, pulmonary artery catheter; pVAD, percutaneous microaxial ventricular assist device; RRT, renal replacement therapy; SMD, standardized mean difference; TIA, transient ischemic attack; VAD, ventricular assist device; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Other includes Unknown, Asian/Pacific Islander, American Indian/Alaska Native, and Other.

Table 2. Associations Between Percutaneous Microaxial Ventricular Assist Device Versus Intra-Aortic Balloon Pump and the Studied Outcomes

Outcomes	Unadjusted cohort		Matching weight analysis		
	pVAD (N=704)	IABP (N=2140)	pVAD (N=645)	IABP (N=639)	Effect estimate
Binary outcomes					aOR (95% CI)
30-d mortality	390 (55.4)	762 (35.6)	355 (55.0)	248 (38.9)	1.92 (1.59– 2.33)
Bleeding	191 (27.1)	641 (30.0)	176 (27.2)	174 (27.1)	1.00 (0.81–1.24)
Stroke	29 (4.1)	78 (3.6)	27 (4.1)	29 (4.5)	0.91 (0.56– 1.47)
Sepsis	56 (8.0)	173 (8.1)	50 (7.7)	54 (8.4)	0.91 (0.64–1.28)
Continuous outcomes					aMD (95% CI)
LOS among survivors, d	12.0 (6.0–21.0)	13.0 (7.0–22.0)	11.0 (6.0–21.0)	12.0 (7.0–20.0)	0.4 (–1.4 to 2.3)
Total health care spending, USD	107 952 (84058–155 769)	58 159 (38998–146 672)	108 426 (83326–155 553)	55 452 (36318–110 533)	*19318 (–11 582 to 50 217)

Values are n (%) or median (25th–75th percentile).

aOR, adjusted odds ratio; aMD, adjusted mean difference; IABP, intra-aortic balloon pump; LOS, length of hospital stay; pVAD, percutaneous microaxial ventricular assist device; and USD, US dollar.

*Hospital was added as fixed-effect to the regression model to estimate the mean difference of the health care spending.

the Danish-German cardiogenic shock (DanGer) trial (NCT01633502) and Early Impella Support in Patients With ST-Segment Elevation Myocardial Infarction Complicated by Cardiogenic Shock (RECOVER IV) trial (NCT05506449) with sample sizes of 360 to 560; however, these RCTs target AMICS, and no RCTs have investigated pVADs for non-AMICS. Meanwhile, some comparative effectiveness studies on AMICS using observational data showed worse prognosis in patients treated with pVADs than those medically managed or treated with IABP,[5–7,15,16] although the interpretations of these studies are subject to unmeasured confounding. A recent study implementing various causal inference methods, such as IV analysis, showed inconsistent results by different analytical approaches and emphasized the importance of adequately powered RCTs.[14]

For non-AMICS, there have been only a few observational studies, the results of which are not consistent.[13,19,37,38] A retrospective multicenter study showed lower mortality with the use of MCS devices than no MCS devices but did not separately evaluate the effectiveness of pVAD.[13] In contrast, an analysis of the National Readmission Database showed an association between the use of pVAD and higher in-hospital mortality in patients with non-AMICS.[19] In our study, similar to the previous studies on AMICS,[5,7,15] all of the analyses using the measured confounding factors showed higher mortality with the use of pVADs. The E-value for the lower end of the CI of 30-day mortality in the principal analysis was 1.83, meaning that unmeasured confounders should be associated with both the treatment and mortality with a risk ratio of 1.83 to nullify the observed association. In other words, if unmeasured confounding variables were as substantial as renal replacement therapy or IMV, the observed higher mortality with the use of pVADs may be nullified. Indeed, we implemented an IV analysis using the cross-sectional institutional preference as the instrument,[14] of which the point estimated for 30-day mortality was closer to 1 compared with other analytical methods. These findings obtained through multiple analytical approaches underscored the significance of unmeasured confounders and the importance of careful study designs when assessing the comparative effectiveness of pVAD in this population. Regardless, it should be noted that the use of pVAD was not associated with lower mortality compared with IABP, necessitating RCTs to validate the causal relationship between the use of pVADs and mortality.

The benefits of MCS devices should always be discussed in the context of complications, such as bleeding. The IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK (IMPRESS) trial showed that the incidence of major bleeding was higher in the pVAD group than in the IABP group.[10] Observational studies also showed higher risks of bleeding in patients with AMICS treated using pVAD compared with those treated using IABP.[5,7] In our study, however, we did not find increased incidences of bleeding in patients treated with pVAD. Generally, patients with acute myocardial infarction receive dual antiplatelet therapy along with revascularization.[39] Because antiplatelet therapy can increase the risk of bleeding, the higher risk of bleeding in patients undergoing pVAD in previous studies targeting AMICS can also be attributed to the addition of antiplatelet therapy to pVAD, which may explain the difference in the association of pVAD with bleeding events between previous studies and the present study. This finding suggested that excess bleeding may not be the only attributable factor of higher mortality with the use of pVAD as reported in previous studies on AMICS.[7,15] Meanwhile, the difference in the safety profile according to the cause of CS can be taken into account when

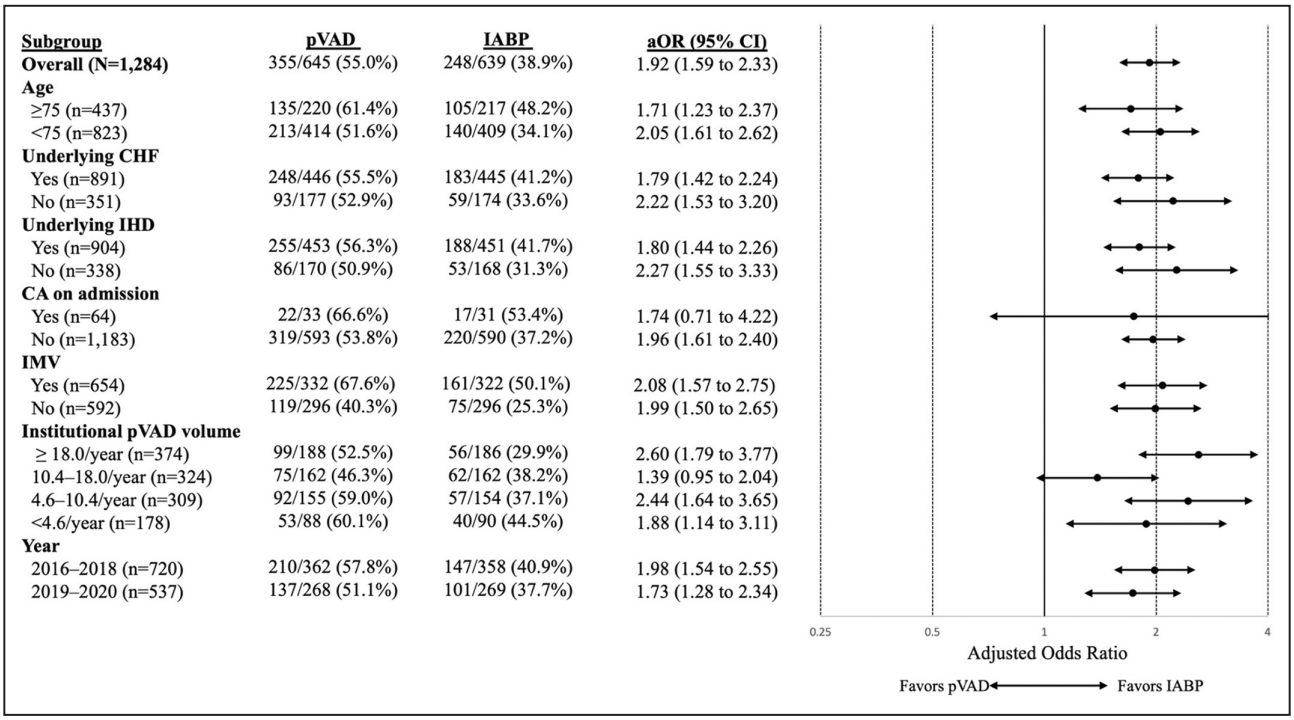

Figure 2. Adjusted odds ratios of the use of pVAD versus IABP for 30-day mortality according to subgroups by matching weight analysis.
Matching weight was performed with complete case analysis. Propensity scores were re-calculated for each subgroup. aOR indicates adjusted odds ratio; CA, cardiac arrest; CHF, congestive heart failure; IABP, intra-aortic balloon pump; IHD, ischemic heart disease; IMV, invasive mechanical ventilation; and pVAD, percutaneous microaxial ventricular assist device.

selecting a treatment strategy, although further studies are needed to clarify this aspect.

Despite the lack of evidence supporting the clinical benefits, the use of pVAD in CS has been increasing over the years.[2,3,5,7] These increases in the use of pVAD prompt careful discussion regarding medical expenses. The use of pVAD has been shown to be significantly associated with increased health care spending in AMICS,[5,7] which may not simply be attributable to longitudinal trends or institutional tendencies.[5,40]

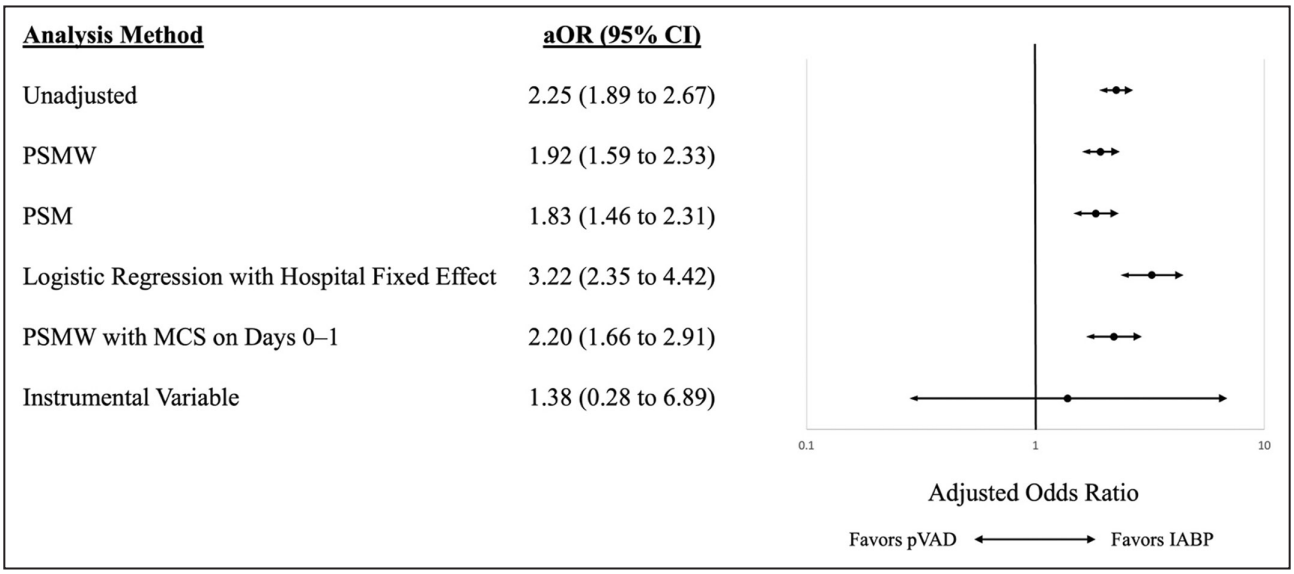

Figure 3. Adjusted odds ratios of the use of pVAD versus IABP for 30-day mortality according to the analysis methods.
aOR indicates adjusted odds ratio; IABP, intra-aortic balloon pump; IHD, ischemic heart disease; MCS, mechanical circulatory support (= pVAD or IABP); PSM, propensity score matching; PSMW, propensity score matching weight; and pVAD, percutaneous microaxial ventricular assist device.

The increases in the use of pVAD have been reported for non-AMICS as well. An observational study using the National Inpatient Sample of the United States reported that the utilization of pVAD among all temporary MCS devices for non-AMICS increased from 0.5% in 2004 to 2007 to 20% in 2015 to 2018.[3] However, the influences of pVAD on health care spending in non-AMICS remain to be investigated. In the current study, we included hospital as a fixed effect to account for the regional and institutional variability in the estimation of health care spending. While the difference in health care spending between the pVAD and IABP groups was not significant in the principal analysis, some subgroup analyses showed significantly higher health care spending with the use of pVAD. Although the association between the use of pVAD and higher health care spending was not definitive from our findings, providers need to be prudent about the setting and indications of pVAD as a treatment for non-AMICS because there is a possibility that the use of pVAD may be associated with increased health care spending in certain situations while not offering much clinical benefit.

LIMITATIONS

Our study had several limitations. First, as is the case for any observational studies, we could not fully account for unmeasured confounding factors. In particular, several clinically relevant factors were unavailable from the claim database, such as left ventricular ejection fraction, serum lactate, or the Society of Cardiovascular Angiography & Interventions CS classification.[41–43] Second, not all of the *ICD-10* codes used for data extraction were validated. For example, although we used the same codes as in a previously published study,[7] and further tested different definitions of bleeding to ensure our findings, the reliability of *ICD-10* codes in identifying the clinical impact of each bleeding event (such as amount or severity) may still be uncertain. Similarly, the sensitivity of the vasopressor use may be underreported, although a previous study using the same database showed similar numbers.[14] Third, although IV analysis could hypothetically overcome unmeasured confounding, the baseline characteristics by the level of institutional pVAD use were not well-balanced, possibly suggesting the violation of the exclusion restriction and exchangeability assumptions.[14] Furthermore, the results of the IV analyses should be interpreted with caution because the relevance of the instrument to the treatment assignment might have led to wide confidence intervals. Fourth, we performed complete case analyses for the assessment of health care spending by linking the 20% random sample Carrier file, which means that our findings regarding health care spending were relatively underpowered. Fifth, our data were not able to distinguish different types of pVAD, such as Impella CP, Impella RP, or Impella 5.5. While they are recorded as the same code in the database, each type has different characteristics, including diameters of the introducers, approaches to access, flow support, and maximum durations of use. For instance, a retrospective study showed that patients treated with Impella 5.5 had lower mortality and higher incidence of the successful bridge to heart replacement therapies than those treated with Impella 5.0,[44] although the observed magnitude would not overturn our findings. Because these differences in devices may affect mortality and risks of complications, further research will be needed to better understand the optimal device choice for these patients.

CONCLUSIONS

This observational study using the Medicare claim database implemented multiple analytical approaches and showed that the use of pVAD compared with IABP was associated with higher mortality in patients with non-AMICS. Adequately powered high-quality RCTs are warranted to determine the clinical effects of pVAD in non-AMICS.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Data S1

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