Title
Intraaortic Balloon Pump vs Peripheral Ventricular Assist Device Use in the United States

Journal
The Annals of Thoracic Surgery, 110(6)

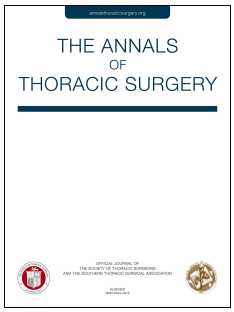
ISSN
0003-4975

Authors
Sanaiha, Yas
Ziaeian, Boback
Antonios, James W
et al.

Publication Date
2020-12-01

DOI
10.1016/j.athoracsur.2020.03.129

Peer reviewed



Intra-aortic Balloon Pump vs Peripheral Ventricular Assist Device Utilization in the US

Yas Sanaiha, MD, Boback Ziaeian, MD PhD, James W. Antonios, Behdad Kavianpour, BS MPH, Ramtin Anousheh, MD, Peyman Benharash, MD

PII: S0003-4975(20)30752-9

DOI: https://doi.org/10.1016/j.athoracsur.2020.03.129

Reference: ATS 33814

To appear in: *The Annals of Thoracic Surgery*

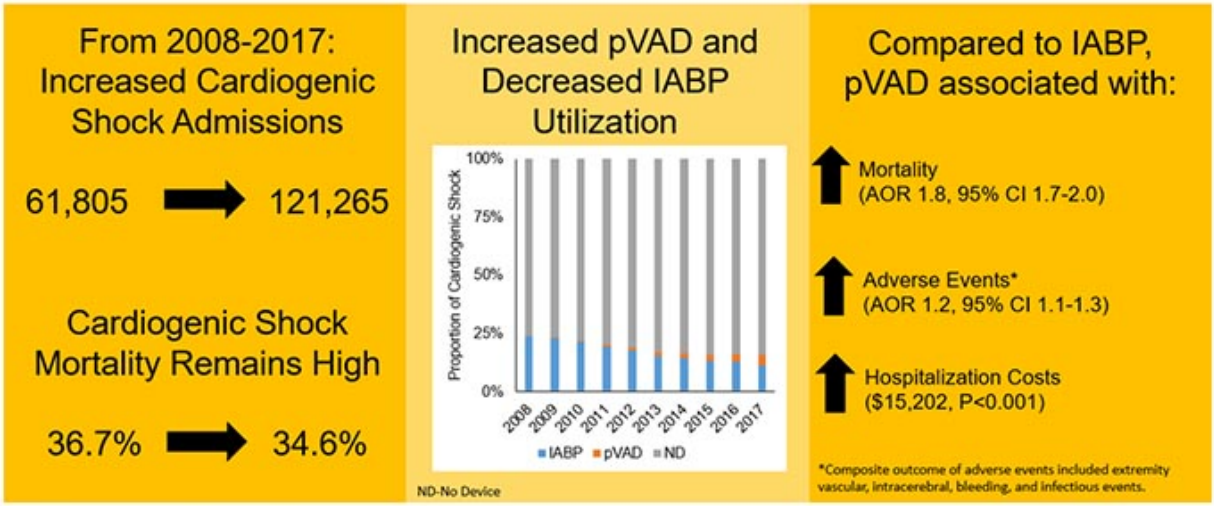
Received Date: 28 October 2019

Revised Date: 26 February 2020

Accepted Date: 31 March 2020

Please cite this article as: Sanaiha Y, Ziaeian B, Antonios JW, Kavianpour B, Anousheh R, Benharash P, Intra-aortic Balloon Pump vs Peripheral Ventricular Assist Device Utilization in the US, *The Annals of Thoracic Surgery* (2020), doi: https://doi.org/10.1016/j.athoracsur.2020.03.129.

Intra-aortic Balloon Pump vs Peripheral Ventricular Assist Device Utilization in the US: Insights from the National Inpatient Sample



THE ANNALS OF THORACIC SURGERY
Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

Sanaiha et al,
The Annals of Thoracic Surgery
@annalsthorsurg

Intra-aortic Balloon Pump vs Peripheral Ventricular Assist Device Utilization in the US

Running Head: IABP vs pVAD in Cardiogenic Shock

Yas Sanaiha MD[1], Boback Ziaeian MD PhD[2,3], James W. Antonios[1], Behdad Kavianpour BS MPH[1], Ramtin Anousheh MD[2], Peyman Benharash MD[1,4]

[1]Cardiovascular Outcomes Research Laboratories (CORELAB)
David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California[1]
[2]Division of Cardiology, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California
[3]Division of Cardiology, Veterans Administration Greater Los Angeles Healthcare System, Los Angeles, California
[4]Division of Cardiac Surgery, University of California, Los Angeles, Los Angeles, California

Address for Correspondence:
Peyman Benharash, MD
Division of Cardiac Surgery
UCLA David Geffen School of Medicine
CHS 62-249, 10833 Le Conte Ave
Los Angeles, CA, 90095
pbenharash@mednet.ucla.edu

Word Count: 4524

Abstract

Background: The objective of the present study was to characterize practical utilization trends and outcomes for intra-aortic balloon pump (IABP) and percutaneous left ventricular assist device (pVAD) in cardiogenic shock at a national level.

Methods: An analysis of all adult patients admitted non-electively for cardiogenic shock from January 2008 through December 2017 was performed using the National Inpatient Sample (NIS). Trends of inpatient IABP and pVAD use were analyzed using survey weighted estimates and the modified Cochran-Armitage test for significance. Multivariable regression models and inverse probability of treatment weights (IPTW) were used to perform risk-adjusted analyses of pVAD mortality a composite of adverse events (AE), and resource utilization, with IABP as reference.

Results: Of an estimated 774,310 patients admitted with cardiogenic shock, 143,051received a device: IABP= 127,792 (16.5%) or pVAD=15,259 (2.0%). The usage of IABP decreased (23.8 to 12.7%, p-for-trend<0.001), while pVAD implantation increased significantly during the study period (0.2 to 4.5%, p-for-trend<0.001). IPTW demonstrated significantly higher odds of mortality with pVAD (OR 1.9, 95% CI 1.7-2.2), but not AE (OR 1.1 95% CI 0.96-1.27) compared to IABP. After risk-adjustment, pVAD use was associated with an additional $15,202 (P<0.001) for survivors and $29,643 for non-survivors (P<0.001).

Conclusions: Over the study period, the rate of pVAD utilization for cardiogenic shock has significantly increased. Compared to IABP, pVAD use was associated with increased mortality, costs and several adverse events. Multi-institutional clinical trials with rigorous inclusion criteria are warranted to evaluate the clinical utility of pVADs in the modern era.

Abbreviations:

pVAD – Peripheral Ventricular Assist Device

IABP- Intra-aortic balloon pump

NIS- National Inpatient Sample

AE- Adverse Event

IPTW- Inverse probability treatment weighting

Despite advances in surgical and medical management, patients with cardiogenic shock suffer high rates of mortality and multi-organ failure.[1–3] While the etiologies of cardiogenic shock are diverse, the ultimate pathophysiologic dysfunction relates to inadequate oxygen delivery and apoptosis or frank necrosis of end organs.[4] Pharmacologic management of this condition via vasoactive agents paradoxically compromises microcirculation and increases myocardial oxygen demand. Elevated intramural cardiac pressures and inadequate coronary perfusion concomitantly worsen cardiac function and peripheral perfusion. Intra-aortic balloon pump (IABP) counterpulsation has demonstrated hemodynamic improvements by reducing myocardial workload and increasing coronary perfusion.[5,6] Despite its widespread use for decades, an eventual randomized control trial (RCT) IABP:SHOCK II trial found no mortality benefit of IABP for patients with cardiogenic shock secondary to acute myocardial infarction at 12 months.[2,7,8]

Technologic advances in catheter design and miniaturization have led to the development of mechanical circulatory support (MCS) devices that may be placed percutaneously. Such next generation percutaneous ventricular assist devices (pVAD) offer observable unloading of the left ventricle and forward aortic flow thereby enhancing coronary perfusion and peripheral hemodynamics.[9,10] Few randomized trials have failed to demonstrate a survival benefit despite improvement in physiologic parameters, while several observational studies have reported conflicting outcomes .[11–14] Khera et al, evaluated the early use of pVAD using a propensity matched national cohort and found its application to be associated with increased complications and similar mortality compared to IABP.[15] Given the absence of definitive data on the efficacy of pVAD, guidelines for appropriate patient selection and its use in cardiogenic shock are lacking.[16–18] Therefore, the present study aimed to evaluate national trends in utilization and risk-

adjusted short-term outcomes for patients in cardiogenic shock receiving either an IABP or pVAD in US hospitals. We hypothesized that pVAD use would be associated with higher mortality, morbidity, and resource utilization.

Patients and Methods

Data Source

We performed a retrospective cross-sectional study of cardiogenic shock patients using the National Inpatient Sample (NIS), the largest, all-payer, nationally representative inpatient database maintained by the Agency for Healthcare Research and Quality.[19] NIS data is generated from state inpatient database discharge abstracts, extracting diagnosis and procedure codes as well as data on hospital bed size, metropolitan versus rural location, teaching status, and region (Supplemental Table 1). Starting in 2012, NIS methodology changed from 100% of discharges to sampling 20% of discharges from participating institutions. Sampling probabilities for each stratum are used to obtain survey estimates representative of nearly 97% of the US population.[20]

Patient Cohort and Variables

We included all adult patient (≥18 years) patients from January 2008 through December 2017 who were admitted non-electively with a diagnosis of cardiogenic shock. Patients were stratified into three treatment groups: pVAD, IABP, or no circulatory support device (Supplemental Table 1). Patients who received both IABP and pVAD, concurrent major cardiac surgery, and extracorporeal membrane oxygenation were excluded from the analysis. Patient comorbidities and procedures were defined using International Classification of Disease (ICD) 9 and 10 administrative diagnostic codes. Frailty was characterized using a previously validated

cluster of frailty-associated diagnoses.[21] Patient transfer status defined as those who were transferred from a different acute care hospital or another type of health care facility using the NIS variable (*TRAN_IN*).

Outcomes of Interest

The primary outcomes of interest was in-hospital mortality. A composite measure of known adverse events (AE) associated with IABP and pVAD arterial cannulation, defined as occurrence of extremity arterial dissection, arterial pseudoaneurysm, limb ischemia, extremity compartment syndrome, fasciotomy, extremity amputation, intracerebral hemorrhage, stroke, retroperitoneal bleed, or septicemia, was included to further compare clinical outcomes (Supplemental Table 1).

Statistical Analysis

Pearson chi-squared tests and adjusted Wald two-tailed t-test were utilized to compare patient and hospital characteristics amongst patients who received IABP versus pVAD accounting for survey weights and NIS design. Unadjusted mortality and AE events are reported in Supplemental Table 2. Annual trends of inpatient IABP and pVAD use, all-cause mortality and AE were analyzed by using survey weighted estimates and the modified Cochran-Armitage test for significance.[22,23] Institutional volume of IABP and pVAD were calculated using unique annual hospital identifiers available in the NIS and plotted for two separate periods, 2008-2011 and 2012-2016, reflecting change from hospital level to patient level analyses in the NIS starting in 2012.

Multivariable regression models were generated to assess predictors of mortality, AE, costs, and LOS based on a review of the literature and known causal factors. The best fit model was selected based on Akaike information criterion (AIC) and Bayesian information criterion. Receiver-operating curve characteristics were also examined for the multivariable models used to assess primary and secondary study outcomes. Models examining mortality, AE, costs, and LOS included the following covariates: Age (treated as curvilinear function using multinomial-fractional polynomials), sex (male gender as reference), history of coronary artery disease, chronic pulmonary parenchymal disease, peripheral vascular disease, diabetes, liver dysfunction, blood or solid organ malignancy, end stage renal disease, electrolyte abnormalities, patient income quartile, primary insurance payer type, hospital type, hospital bed capacity, patient reported race, hospital region, transfer status, frailty status, concomitant percutaneous coronary intervention (PCI) during index hospitalization, in addition to categories of cardiogenic shock. The potential etiologies of cardiogenic shock considered included: acute myocardial infarction, cardiomyopathy, valvular disease, cardiac arrest, complications of myocardial infarction, and arrhythmias.

We used inverse probability of treatment weights (IPTW) to address potential treatment selection bias. Using a model including the above-listed covariates in addition to the NIS level discharge patient weight, we performed a multi-level mixed-effects logistic regression to predict device selection. Propensity scores were generated based off this model and used to generate inverse probability treatment weights. The inverse probability treatment weight was used to modify the NIS provided DISCWT and generate a new weight for survey-weighted analyses (ATE-IPTW). Subsequently, logistic regression analysis of mortality and AE was performed using the ATE-IPTW assigned weight.[24,25] Multivariable models including surgical patients and

excluding patients in the era prior to 2012 were also performed with the models described above and reported to demonstrate the association of pVAD with cardiogenic shock outcomes, regardless of surgical patients and procedural era.

The NIS provides total hospitalization charges, which were converted to costs using the NIS cost-to-charge ratio files. Cost adjustment is performed using the Medicare Expenditure Personal Heath Care Index , with 2017 as the reference year.[26] Non-parametric trend analysis were performed for unadjusted costs and LOS. Using log-transformed linear regression and exponentiation, we obtained incremental costs associated with pVAD compared to IABP. Incremental LOS associated with pVAD was also evaluated using linear regression. This study was deemed exempt by the institutional review board at the University of California, Los Angeles and Stata 15.1 (Statacorp, College Station, TX) software was used to perform all statistical analyses.

Results

Over the study period, the annual number of cardiogenic shock related admissions significantly increased from 61,805 to 121,265, with a reduction in overall mortality from 36.7% to 34.6% (p-for-trend<0.001) (Figure 1). Of an estimated 774,310 patients admitted with cardiogenic shock who met inclusion criteria, 143,051 received a device: IABP= 127,792 (16.5%), pVAD= 15,259 (2.0%) (Figure 2). Compared to the IABP cohort, pVAD patients were younger, more commonly male, and had a higher prevalence of diabetes, liver disease, and heart failure, among others (Table 1). PVAD implantation was more commonly performed at metropolitan-teaching hospitals. Furthermore, patients with cardiogenic shock at rural and non-teaching facilities were more likely to receive IABP rather than pVAD (Table 1). The proportion

of acute myocardial infarction patients was greater in the IABP cohort compared to pVAD (Table 1).

Usage of IABP decreased (23.8 to 12.7%, p-for-trend<0.001), while pVAD implantation (0.2 to 3.5%, p-for-trend<0.001) and those treated without a device (76.1 to 83.8%, p-for-trend <0.001) increased significantly during the study period (Figure 3). The number of hospitals using pVAD also increased significantly, while IABP application showed a steady trend in both eras of NIS sampling methodology (Figure 4). Furthermore, we observed a wide variation in the proportion of cardiogenic shock patients treated with pVAD by hospital (Figure 5). Over the study period, the mortality for IABP and pVAD did not exhibit a significant change (IABP p-for-trend=0.87, pVAD p-for-trend=0.28) (Figure 6).

Unadjusted all-cause mortality (44.9 vs 32.0%, P<0.001) and rate of adverse events (AE) (11.1 vs 6.8%, P<0.001) were significantly higher for patients who received pVAD compared to IABP (Supplemental Table 2). After adjusting for patient and hospital characteristics using multivariable single-level regression, pVAD was associated with nearly two-fold increase in mortality (OR 1.85, 95% CI 1.69-2.02, P<0.001) and 16% higher odds of AE (OR 1.16, 95% CI 1.05-1.29, P<0.001) with IABP as reference (Table 2). Sensitivity analysis including patients that underwent coronary artery or valve operations demonstrated and restricting the analysis to the 2012-2017 era demonstrated concordant results (Table 2). After application of inverse probability weights, multivariable analysis confirmed significantly higher odds of mortality (OR 1.93, 95% CI 1.67-2.23, P<0.001), but not AE (1.10 95% CI 0.96-1.27, P<0.001) for pVAD compared to IABP (Table 2).

Over the study period, for both survivors and non-survivors of cardiogenic shock, costs and LOS remained comparable (Figure 7). Compared to IABP, pVAD use was associated with

higher unadjusted costs ($84,433 vs $54, 509, P<0.001) and longer average length of stay (11.0vs 10.3 days, P=0.03). After risk-adjustment for baseline comorbidities and hospital characteristics, pVAD use was associated with an additional $15,202 (P<0.001) for survivors and $29,643 for non-survivors (P<0.001). Risk-adjusted LOS was similar for both support modalities.

Comment

Mechanical circulatory devices are increasingly used to support the failing heart in both acute and chronic circumstances. Despite the use of inotropes and IABP for its treatment, cardiogenic shock continues to incur a high mortality. Traditional ventricular assist devices are used to treat patients with end stage heart disease and remain limited in use owing to their form factor and surgical implantation risks. The bulky, extracorporeal pumps of the past decade have now been replaced with counterparts that can be implanted within the chest cavity or inserted percutaneously for single ventricular dysfunction. Introduction of pVAD devices has altered the landscape of short-term support for cardiogenic shock with studies demonstrating improvements in hemodynamics.[9,27] In this nationwide study of IABP and pVAD use in patients hospitalized with cardiogenic shock, we found a dramatic increase (from 0.2 to 3.5%) in pVAD and significant decline in IABP use. While the overall mortality for cardiogenic shock remained steady, use of pVAD was associated with increased mortality, costs, and a trend towards increased complications. Several of our findings warrant further discussion

Our observation of increased pVAD use is consistent with previously reported national trends. Several studies have reported increases in pVAD utilization ranging from 300-1151% from 2007-2012 for various indications.[28,29] The hasty growth in pVAD use was preceded by a

single randomized clinical trial comparing IABP and Impella in cardiogenic shock.[11] This study of 12 pVAD and 13 IABP patients demonstrated marginal improvements in cardiac index and decreased vasopressor use with Impella but no difference in mortality.[11] Since this initial publication, additional trials, such as PROTECT II in high-risk PCI patients, have found similar incidence of 30-day major adverse events between Impella 2.5 and IABP, with trends for improved outcomes in the pVAD cohort at 90 days.[30] Several institutional retrospective registry studies have also demonstrated decreased need for blood transfusions with IABP compared to pVAD, however significant evidence for mortality benefit is lacking [16,31,32]. In the present study, patients receiving pVADs were on average younger, appeared healthier, with lower myocardial infarction rates compared to the IABP cohort. However, these patients endured worse outcomes, an observation that could only be verified in randomized prospective trials.

The rapid adoption of pVAD technology is not unexpected given the ease of implant compared to prior generations of percutaneous support devices, which required trans-septal puncture. Nonetheless, wide variations in pVAD use warrants further investigation. If pVAD utilization was driven primarily by patient factors, a more consistent pattern would be expected. However, our present analysis shows no such relationship between institutional volume of cardiogenic shock admissions requiring mechanical circulatory support and pVAD utilization. These findings underscore the inconsistencies in real-world pVAD utilization, which are particularly concerning given the evidence for improved survival with increased institutional pVAD volume for myocardial infarction and cardiogenic shock.[33] With increased adoption of this technology, investigation of minimal volume standards is warranted and may improve deployment of pVAD in hospitals with infrastructure and nursing expertise to safely monitor such patients.

The present study has several important limitations, inherent to its retrospective nature. First, hemodynamic and vasopressor information is not available, thus limiting our ability to assess the severity of cardiogenic shock. By using the largest national inpatient database, we were able to generate a large cohort of patients admitted with cardiogenic shock requiring mechanical device support. However, we are unable to monitor long-term outcomes.-Type of pVAD device and duration of IABP and pVAD support cannot be discerned within our database. Furthermore, adverse events are attributed to device use, but it is important to recognize that these events cannot clearly be distinguished from comorbidities due to limitations of ICD coding. Duration of device utilization was also not feasible until the ICD10 era, and thus we cannot adjust for this important factor in our analysis. Nonetheless, the present study provides contemporary data on practical utilization patterns and outcomes.

In summary, in this large, nationally representative cohort, we found pVAD use in cardiogenic shock to be associated with increased mortality, costs and several adverse events including septicemia, bleeding, and vascular complications. While such differences may be attributed to factors unaccounted for in the database, we used inverse probability weighted analysis, a robust method to account for differences in patient characteristics, to explicitly adjust for several comorbidities between the IABP and pVAD groups. Our findings highlight the ambiguity surrounding the benefits of pVAD devices in patients with cardiogenic shock. Multi-institutional randomized clinical trials with rigorous inclusion criteria are warranted to scrutinize the clinical utility of pVADs in real-world practice.

References:

1. Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J. Thirty-Year Trends (1975 to 2005) in the Magnitude of, Management of, and Hospital Death Rates Associated With Cardiogenic Shock in Patients With Acute Myocardial Infarction. Circulation. 2009;119(9):1211-1219. doi:10.1161/CIRCULATIONAHA.108.814947

2. Thiele H, Zeymer U, Thelemann N, et al. Intraaortic Balloon Pump in Cardiogenic Shock Complicating Acute Myocardial Infarction. Circulation. 2019;139(3):395-403. doi:10.1161/CIRCULATIONAHA.118.038201

3. Nguyen HL, Yarzebski J, Lessard D, Gore JM, McManus DD, Goldberg RJ. Ten□Year (2001–2011) Trends in the Incidence Rates and Short□Term Outcomes of Early Versus Late Onset Cardiogenic Shock After Hospitalization for Acute Myocardial Infarction. J Am Heart Assoc. 2017;6(6). doi:10.1161/JAHA.117.005566

4. Thiele H, Ohman EM, Desch S, Eitel I, de Waha S. Management of cardiogenic shock. Eur Heart J. 2015;36(20):1223-1230. doi:10.1093/eurheartj/ehv051

5. Scheidt S, Wilner G, Mueller H, et al. Intra-Aortic Balloon Counterpulsation in Cardiogenic Shock. N Engl J Med. 1973;288(19):979-984. doi:10.1056/NEJM197305102881901

6. Prondzinsky R, Unverzagt S, Russ M, et al. Hemodynamic Effects of Intra-aortic Balloon Counterpulsation in Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock. Shock. 2012;37(4):378-384. doi:10.1097/SHK.0b013e31824a67af

7. Thiele H, Zeymer U, Neumann F-J, et al. Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock. N Engl J Med. 2012;367(14):1287-1296. doi:10.1056/NEJMoa1208410

8. Thiele H, Zeymer U, Neumann F-J, et al. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet. 2013;382(9905):1638-1645. doi:10.1016/S0140-6736(13)61783-3

9. Remmelink M, Sjauw KD, Henriques JPS, et al. Effects of mechanical left ventricular unloading by impella on left ventricular dynamics in high-risk and primary percutaneous coronary intervention patients. Catheter Cardiovasc Interv. 2010;75(2):187-194. doi:10.1002/ccd.22263

10. Watanabe S, Fish K, Kovacic JC, et al. Left Ventricular Unloading Using an Impella CP Improves Coronary Flow and Infarct Zone Perfusion in Ischemic Heart Failure. J Am Heart Assoc. 2018;7(6). doi:10.1161/JAHA.117.006462

11. Seyfarth M, Sibbing D, Bauer I, et al. A Randomized Clinical Trial to Evaluate the Safety and Efficacy of a Percutaneous Left Ventricular Assist Device Versus Intra-Aortic Balloon Pumping for Treatment of Cardiogenic Shock Caused by Myocardial Infarction. J Am Coll Cardiol. 2008;52(19):1584-1588. doi:10.1016/j.jacc.2008.05.065

12. Ouweneel DM, Engstrom AE, Sjauw KD, et al. Experience from a randomized controlled trial with Impella 2.5 versus IABP in STEMI patients with cardiogenic pre-shock. Lessons learned from the IMPRESS in STEMI trial. Int J Cardiol. 2016;202:894-896. doi:10.1016/j.ijcard.2015.10.063

13. Ouweneel DM, Eriksen E, Sjauw KD, et al. Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction. J Am Coll Cardiol. 2017;69(3):278-287. doi:10.1016/j.jacc.2016.10.022

14. Alushi B, Douedari A, Froehlig G, et al. Impella versus IABP in acute myocardial infarction complicated by cardiogenic shock. Open Hear. 2019;6(1):e000987. doi:10.1136/openhrt-2018-000987

15. Khera R, Angraal S, Couch T, et al. Adherence to Methodological Standards in Research Using the National Inpatient Sample. JAMA. 2017;318(20):2011-2018. doi:10.1001/jama.2017.17653

16. Schrage B, Ibrahim K, Loehn T, et al. Impella Support for Acute Myocardial Infarction Complicated by Cardiogenic Shock. Circulation. 2019;139(10):1249-1258. doi:10.1161/CIRCULATIONAHA.118.036614

17. Ouweneel DM, Eriksen E, Sjauw KD, et al. Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction. J Am Coll Cardiol. 2017;69(3):278-287. doi:10.1016/j.jacc.2016.10.022

18. Thiele H, Jobs A, Ouweneel DM, et al. Percutaneous short-term active mechanical support devices in cardiogenic shock: a systematic review and collaborative meta-analysis of randomized trials. Eur Heart J. 2017;38(47):3523-3531. doi:10.1093/eurheartj/ehx363

19. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). 2006-2009. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/databases.jsp.

20. Khera R, Krumholz HM. With Great Power Comes Great Responsibility. Circ Cardiovasc Qual Outcomes. 2017;10(7):e003846. doi:10.1161/CIRCOUTCOMES.117.003846

21. Tran DTT, Tu J V., Dupuis JY, Eddeen AB, Sun LY. Association of frailty and long-term survival in patients undergoing coronary artery bypass grafting. J Am Heart Assoc. 2018;7(15). doi:10.1161/JAHA.118.009882

22. Klein RJ, Schoenborn CA. Age Adjustment Using the 2000 Projected U.S. Population. https://www.cdc.gov/nchs/data/statnt/statnt20.pdf. Accessed January 5, 2018.

23. Royston P. PTREND: Stata module for trend analysis for proportions. Stat Softw Components. October 2014. https://ideas.repec.org/c/boc/bocode/s426101.html. Accessed January 15, 2018.

24. DuGoff EH, Schuler M, Stuart EA. Generalizing Observational Study Results: Applying Propensity Score Methods to Complex Surveys. Health Serv Res. 2014;49(1):284-303. doi:10.1111/1475-6773.12090

25. Zhou T. Robust Methods for Causal Inference Using Penalized Splines. 2018. https://deepblue.lib.umich.edu/handle/2027.42/147507. Accessed April 12, 2019.

26. Using Appropriate Price Indices for Expenditure Comparisons. https://meps.ahrq.gov/about_meps/Price_Index.shtml. Accessed May 18, 2019.

27. Burzotta F, Trani C, Doshi SN, et al. Impella ventricular support in clinical practice: Collaborative viewpoint from a European expert user group. Int J Cardiol. 2015;201:684-691. doi:10.1016/J.IJCARD.2015.07.065

28. Khera R, Cram P, Lu X, et al. Trends in the Use of Percutaneous Ventricular Assist Devices. JAMA Intern Med. 2015;175(6):941. doi:10.1001/jamainternmed.2014.7856

29. Stretch R, Sauer CM, Yuh DD, Bonde P. National Trends in the Utilization of Short-Term Mechanical Circulatory Support. J Am Coll Cardiol. 2014;64(14):1407-1415. doi:10.1016/j.jacc.2014.07.958

30. O'Neill WW, Kleiman NS, Moses J, et al. A Prospective, Randomized Clinical Trial of Hemodynamic Support With Impella 2.5 Versus Intra-Aortic Balloon Pump in Patients

Undergoing High-Risk Percutaneous Coronary Intervention. Circulation. 2012;126(14):1717-1727. doi:10.1161/CIRCULATIONAHA.112.098194

31. Lamarche Y, Cheung A, Ignaszewski A, et al. Comparative outcomes in cardiogenic shock patients managed with Impella microaxial pump or extracorporeal life support. J Thorac Cardiovasc Surg. 2011;142(1):60-65. doi:10.1016/J.JTCVS.2010.07.075

32. Boudoulas KD, Pederzolli A, Saini U, et al. Comparison of Impella and intra-aortic balloon pump in high-risk percutaneous coronary intervention: Vascular complications and incidence of bleeding. Acute Card Care. 2012;14(4):120-124. doi:10.3109/17482941.2012.741244

33. O'Neill WW, Grines C, Schreiber T, et al. Analysis of outcomes for 15,259 US patients with acute myocardial infarction cardiogenic shock (AMICS) supported with the Impella device. Am Heart J. 2018;202:33-38. doi:10.1016/J.AHJ.2018.03.024

Table 1. Comparison of Patient Demographics and Hospital Characteristics for patients admitted with cardiogenic shock.

	IABP	PVAD	P-Value	ND
	N=127,792 (%)	N=15,259 (%)		N=631,259 (%)
Age (median, IQR years)	65 (56-75)	65 (56-73)	<0.001	69 (59-80)
Female	32.8	28.7	<0.001	41.7
Coronary Artery Disease	69.5	62.7	<0.001	41.1
Chronic Pulmonary Parenchymal Disease	18.1	15.0	0.001	25.2
Hypertension	50.6	53.2	0.024	51.1
Peripheral Vascular Disease	7.3	8.6	<0.001	9.8
Frailty	10.2	11.1	<0.001	19.7
Diabetes	27.9	26.4	<0.001	26.2
Chronic Liver Dysfunction	15.2	22.1	<0.001	17.0
Substance Abuse	5.1	4.9	<0.001	6.6
End Stage Renal Disease	17.1	21.5	<0.001	29.2
Coagulopathy	12.7	17.9	<0.001	14.2
Electrolyte	46.6	53.2	<0.001	55.9
Cancer	1.8	1.4	<0.001	3.7
Transfer	23.3	30.1	<0.001	20.7
Percutaneous Coronary Intervention	66.3	63.3	<0.001	13.4
Acute Myocardial Infarction	57.2	38.8	<0.001	16.7
Myocardial Infarction Complication	1.8	1.2	<0.001	0.4
Valvular Disease	10.5	8.8	0.0043	10.0
Myocarditis	0.3	1.0	<0.001	0.2
Cardiomyopathy	60.4	71.6	<0.001	66.4
Arrhythmia	64.3	61.8	<0.001	58.4
Pericardial disease	3.0	3.3	0.0102	3.4
Cardiac Arrest	22.5	20.1	<0.001	17.5
Race			<0.001	
White	72.9	71.9		69.3
Black	9.9	12.0		15.5
Hispanic	8.5	8.2		8.2
Asian	3.5	2.4		3.1
Other/Unknown	5.17	5.46		3.9
Insurance Type			<0.001	
Medicare	52.9	52.2		65.8
Medicaid	9.5	10.4		10.2
Private	28.0	28.6		17.4
Self-Pay	6.3	5.3		3.9
Other/Unknown	3.26	3.51		2.7
Income Quartile			<0.001	
0-25th percentile	27.0	30.9		30.7
26-50th percentile	26.3	27.0		26.2
51-75th percentile	24.6	23.6		23.5
76-100th percentile	22.1	18.6		19.7
Region			<0.001	
Northeast	18.2	15.3		18.1
Midwest	24.1	18.1		20.5
South	36.9	44.2		38.9
West	20.8	22.4		22.5
Bedsize			<0.001	
Small	8.5	8.3		10.8
Med	22.7	24.2		24.3

Large	68.8	67.6		64.9
Teaching Status			<0.001	
Rural	4.7	2.6		5.8
Metro/Non-teach	32.1	21.1		29.2
Metro/Teach	63.2	76.3		65.0

Legend: IABP- intra-aortic balloon pump, IQR- Interquartile Range, Metro-Metropolitan, ND- no device utilized, pVAD- percutaneous ventricular assist device.

Table 2. Risk-Adjusted Analysis of Primary and Secondary Outcomes using single- and inverse probability treatment weight two-level analyses.

	AOR Mortality	95% CI	AOR AE	95% CI
Model 1:	1.85	1.69-2.02	1.16	1.05-1.29
Model 2:	1.85	1.72-2.04	1.15	1.01-1.32
Model 3:	1.24	1.13-1.37	1.13	0.98-1.30
Model 4:	1.93	1.68-2.23	1.11	0.96-1.27

Model 1: Single level, logistic regression
Model 2: Single level, logistic regression including CT Surgery
Model 3: Single level, logistic regression, restricted to 2012-2017 era
Model 4: Inverse Probability Treatment Weighting derived from multi-level mixed effects model

AOR- Adjusted odds ratio, AE- Composite Adverse Event Variable, CI- Confidence Interval, IPTW- Inverse

Figure Legends:

Figure 1. Trend of Cardiogenic Shock Hospitalizations and Overall Mortality. Blue line represents mortality rate for all-cause cardiogenic shock admissions. Error bars represent standard error. Orange line represents survey-weighted cardiogenic shock admissions. P-for-trend <0.001.

Figure 2. Study consort Diagram with survey-weighted estimates.

Figure 3. Trends of IABP and pVAD Trend. Blue line represents rate of IABP utilization for all cardiogenic shock admissions. Orange line represents rate of pVAD utilization for all cardiogenic shock admissions. Gray-bars represent proportion of cardiogenic shock admissions not receiving either IABP or pVAD (No device- ND).

Figure 4. Institutions performing pVAD (A) or IABP (B) for Cardiogenic Shock. Blue bars represent number of hospitals performing IABP. Orange bars representing number of hospitals performing pVAD. *Starting in 2012, NIS methodology changed from hospital level to patient level sampling.

Figure 5. Proportion of pVAD utilization compared to total IABP and pVAD institutional volume. Blue line represents pVAD proportion of all cardiogenic shock admissions requiring either pVAD or IABP, orange bars represent annual institutional IABP and pVAD volume

Figure 6. Mortality of Cardiogenic Shock with or without mechanical circulatory support device. ND- No device used in management of cardiogenic shock. Error bars represent Standard Error. IABP Mortality p-for-trend=0.08, pVAD Mortality p-for-trend=0.22, ND p-for-trend <0.001. IABP AE p-for-trend 0.96 for pVAD AE p-for-trend<0.001.

Figure 7. Costs and LOS for Survivor and Non-Survivors of IABP, pVAD, and No-Device Cardiogenic Shock Patients. ND- No device used in management of cardiogenic shock. Error bars represent Standard Error. P-for-trend <0.001 only for ND Survivors and Non-Survivors. No significant trend for IABP or PVAD