Predictors of Mortality and Outcomes of Acute Severe Cardiogenic Shock Treated with the Impella Device

Charlene L. Rohm, MD[a,*], Bogdan Gadidov, PhD[b], Michael Leitson, MSAS[c], Herman E. Ray, PhD[b,d], and Rajnish Prasad, MD[e]

The Impella (Abiomed, Danvers, Massachusetts) device is increasingly used for mechanical circulatory support (MCS) to treat acute severe cardiogenic shock (CS). Initial and continued determination of the appropriate degree of MCS is challenging. This study evaluates predictors of mortality in patients treated with the Impella for acute severe CS and outcomes associated with prolonged Impella use. This retrospective single-center study included 204 patients treated with the Impella 2.5, Impella CP, or Impella 5.0 from 2011 to 2018 for acute severe CS. The primary end point was all-cause in-hospital mortality. All-cause in-hospital mortality was 45.1%. Nonsurvivors had a lower initial pH (7.24 vs 7.32, hazard ratio [HR] 1.03, p <0.0001), lower serum CO_2 (19.1 vs 21.3 mmol/L, HR 1.08, p = 0.002), higher lactate (6.8 vs 3.3 mmol/L, HR 1.17, p <0.0001), and used a greater number of vasopressors and inotropes (4.3 vs 2.6, HR 1.44, p <0.0001). Patients with the Impella >4 days (n = 45) had a longer intensive care unit stay (12.6 vs 6.9 days, p <0.001), longer total hospital stay (16.4 vs 11.6 days, p = 0.03), longer mechanical ventilation use (7.8 vs 4.4 days, p = 0.002), and trend toward increased mortality (57.8 vs 41.5%, p = 0.051). In conclusion, in patients treated with the Impella for acute severe CS, initial biochemical parameters and need for vasopressors and inotropes are significant predictors of mortality that can serve as valuable indicators of whether the Impella or higher level of MCS is more appropriate. Patients treated with the Impella beyond 4 days have poorer outcomes and may benefit from escalation of care. **(Am J Cardiol 2019;124:499−504)**

The increased use of evidence-based medical therapy and interventions has reduced hospital mortality rates for patients with cardiogenic shock (CS).[1] Multiple retrospective studies have shown improved hemodynamics and survival with the Impella (Abiomed, Danvers, Massachusetts).[2−9] These favorable outcomes have led to increased use of the Impella for mechanical circulatory support (MCS) in treating acute severe CS. However, the initial and continued determination of the appropriate level of MCS during hospitalization remains challenging. The Impella 2.5, Impella CP, Impella 5.0, and Impella LD Catheters are intended for short-term use (≤4 days for Impella 2.5 and CP; ≤6 days for Impella 5.0 and LD) to treat acute refractory CS.[10] Despite these recommendations, prolonged use of the Impella in the treatment of CS has been observed with unknown outcomes. This study evaluates predictors of mortality in patients treated with the Impella for acute severe CS and outcomes associated with prolonged Impella use (>4 days).

Methods

This study was approved by Western Institutional Review Board (WIRB, study number 1170792). A retrospective analysis was conducted of all patients treated with the Impella 2.5, Impella CP, or Impella 5.0 from 2011 to 2018 at a single institution for hemodynamic support in acute severe CS. Patients treated with the Impella 2.5, Impella CP, or Impella 5.0 for acute severe CS were included. Severe CS was defined as a systolic blood pressure <90 mm Hg for at least 30 minutes or the need for vasopressors or inotropes to maintain a systolic blood pressure ≥90 mm Hg. Patients who received the Impella for high-risk percutaneous coronary intervention or after starting venoarterial extracorporeal membrane oxygenation were excluded. Patient baseline characteristics were obtained through review of the electronic medical record. Preimplantation parameters were defined as initial values before the use of the Impella.

The primary end point was all-cause in-hospital mortality, defined as death from all causes during index hospitalization. Death included natural death, withdrawal of care leading to death, and discharge to hospice. Survivors were defined as those patients with successful explantation of the Impella and discharge to either home or a rehabilitation facility.

t Tests were used to compare means of continuous variables for the outcome of mortality. To test for differences in probability of mortality across groups, binomial tests of proportions were performed. The Cochran-Armitage test is used to test for a monotonic trend in proportions. Univariate Cox proportional hazards models were used to generate hazard ratios (HR) for each predictor of mortality. The total

[a]Department of Internal Medicine, WellStar Kennestone Regional Medical Center, Marietta, Georgia; [b]Analytics and Data Science Institute, Kennesaw State University, Kennesaw, Georgia; [c]Institutional Research, University of North Georgia, Dahlonega, Georgia; [d]Department of Statistics and Analytical Sciences, Kennesaw State University, Kennesaw, Georgia; and [e]WellStar Cardiovascular Medicine, WellStar Kennestone Regional Medical Center, Marietta, Georgia. Manuscript received March 11, 2019; revised manuscript received and accepted May 7, 2019.

See page 503 for disclosure information.

*Corresponding author: Tel: 770-880-2929.

E-mail address: charlene.rohm@wellstar.org (C.L. Rohm).

0002-9149/
https://doi.org/10.1016/j.amjcard.2019.05.039

hospital length of stay (days) was used as the time-to-event variable in all survival analyses. Individual Kaplan-Meier curves were constructed for lactate, pH, serum CO_2, and total number of vasopressors and inotropes used. The Kaplan-Meier curves were stratified according to the quartiles of each predictor. The log-rank test was used to test for significant survival differences, with the Bonferroni method used to adjust the p-value for multiple comparisons. A significance level of 0.05 was used for all tests. SAS version 9.4 was used for all analyses. Kaplan-Meier curves were generated from JMP Pro 13.

Results

A total of 204 patients received the Impella for treatment of acute severe CS from March 2011 to July 2018 at a single institution. Table 1 shows baseline characteristics. The etiology of acute severe CS included 112 (54.9%) patients with ST-elevation myocardial infarction, 50 (24.5%) with non ST-elevation myocardial infarction, 27 (13.2%) with cardiac arrest, 7 (3.4%) with ischemic cardiomyopathy, 4 (2.0%) with nonischemic cardiomyopathy, and 4 (2.0%) with acute myocarditis.

All but 4 patients required at least 1 vasopressor or inotrope before receiving the Impella. Vasopressors and inotropes were initiated within the first 24 hours of cardiogenic shock. The mean ± standard deviation (SD) number of vasopressors or inotropes used was 3.4 ± 1.6 (range of 0 to 7). The vasopressors used included norepinephrine (administered to 90% of patients), epinephrine (41% of patients), vasopressin (39% of patients), phenylephrine (60% of patients), and dopamine (22% of patients). Inotropes included milrinone (28% of patients) and dobutamine (56% of patients). One hundred thirty-seven patients (67%) received vasopressor and inotrope combinations. One hundred forty-one (69%) received only vasopressors whereas 4 (2%) received only inotropes. The mean ± SD number of vasopressors and inotropes used was 3.4 ± 1.6 (range of 0 to 7).

Table 1
Baseline Characteristics (n = 204)

Demographics and comorbidities		
Age (years)	60.3 ± 12.0	62.5 (16.3)
Male sex	145 (71.1%)	
White	153 (75.0%)	
Black	33 (16.2%)	
Hispanic	11 (5.4%)	
Asian	7 (3.4%)	
Coronary artery disease	177 (86.8%)	
Hypertension	146 (71.6%)	
Current or prior smoker	119 (58.3%)	
Hypercholesterolemia	109 (53.4%)	
Diabetes mellitus	99 (48.5%)	
Obesity (body mass index ≥30 kg/m^2)	86 (42.4%)	
Congestive heart failure	51 (25.0%)	
Previous myocardial infarction	30 (14.7%)	
Alcohol abuse	25 (12.3%)	
Chronic obstructive pulmonary disease	22 (10.8%)	
Stroke	22 (10.8%)	
End stage renal disease	5 (2.5%)	
Illicit drug use	6 (2.9%)	
Pre-Impella hemodynamic and biochemical parameters		
Admitting left ventricular ejection fraction (%)	21.5 ± 11.7	20 (10)
Initial Fick cardiac index (L/min/m^2)	1.9 ± 0.7	1.8 (0.6)
Initial pulmonary capillary wedge pressure (mm Hg)	26.5 ± 9.3	26 (11.5)
Initial lactate (mmol/L)	5.2 ± 4.1	3.7 (4.8)
Initial pH	7.28 ± 0.14	7.3 (0.18)
Initial CO_2 (mmol/L)	20.3 ± 4.7	20 (6)
Initial SVO_2 (%)	55.3 ± 15.8	57 (20.8)
Vasopressors and inotropes used	3.4 ± 1.6	3 (3)

Values are mean ± SD with median (IQR), or n (%).
Hypertension defined as ≥140/90 mm Hg.
Hypercholesterolemia defined as total cholesterol ≥200 mg/dl or low-density lipoprotein ≥100 mg/dl.

Fifty-five (27%) patients received the Impella 2.5, 143 (70%) received the Impella CP, and 6 (3%) received the Impella 5.0. The mean ± SD duration of Impella use was 3.2 ± 2.4 days (range of 2 hours to 15 days). One hundred fifty-nine patients (77.9%) required endotracheal intubation and mechanical ventilation. The median (interquartile range [IQR]) duration of mechanical ventilation was 3 (6) days (range of 3 hours to 37 days). The median (IQR) duration of intensive care unit stay was 6 (8.3) days (range of 3 hours to 54 days). The median (IQR) duration of total hospital stay was 9 (12.5) days (range of 3 hours to 59 days).

Although 204 patients were included, some initial hemodynamic and biochemical parameters were incomplete. Appendix A shows the percentage of complete observations for each initial parameter. The ability to perform a multivariate analysis was limited due to the incomplete nature of the data, with only 31% of patients with all 4 covariates. Data on total number of vasopressors and inotropes was available for all 204 patients.

All-cause mortality during index hospitalization was 45.1%. Figure 1 shows that nonsurvivors (n = 92) compared with survivors had a statistically significant higher initial lactate (6.8 vs 3.3 mmol/L, HR 1.17, p <0.0001), lower initial pH (7.24 vs 7.32, HR 1.03, p <0.0001), lower initial serum CO_2 (19.1 vs 21.3 mmol/L, HR 1.08, p = 0.002), and used a greater number of vasopressors and inotropes (4.3 vs 2.6, HR 1.44, p <0.0001). There was a statistical difference in the initial SVO_2 between nonsurvivors and survivors (51.1 vs 59.9%, p <0.0001). However, the HR of 1.013 did not demonstrate statistical significance (p = 0.098). Initial SVO_2 was the least complete initial predictor (Appendix A), which is likely the reason for a nonsignificant HR. The HRs for the initial predictors are presented in Figure 1. A complete table with *t* Tests for each initial predictor and other covariates is shown in Appendix B, with HRs and 95% confidence intervals (CI) presented in Appendix C.

The median survival of patients with initial lactate quartile ranges of ≤2.0 mmol/L, 2.1 to 3.7, 3.8 to 6.9, and >6.9 was 46 days, 32 days, 9 days, and 4 days, respectively (Figure 2). The initial lactate range was 0.7 to 18.6 mmol/L. The median survival of patients with initial pH quartile ranges of ≤7.21, 7.22 to 7.31, 7.32 to 7.39, and >7.39 was 6 days, 13 days, 32 days, and 46 days, respectively (Figure 2). The range in pH was 6.86 to 7.56. The median survival of patients with initial serum CO_2 quartile ranges of ≤17 mmol/L, 17.1 to 20, 20.1 to 24, and >24 was 6 days, 33 days, 40 days, and 22 days, respectively (Figure 2). The initial serum CO_2 range was 7 to 38 mmol/L.

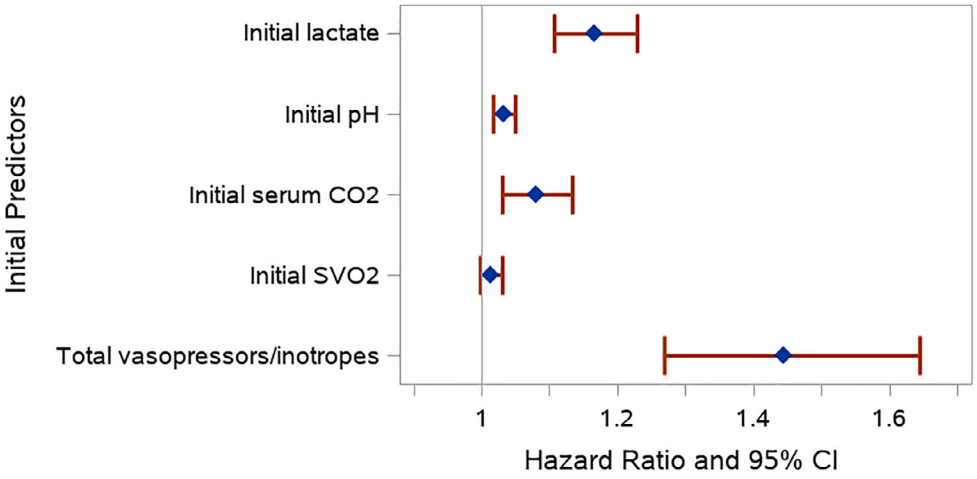

Figure 1. Initial Predictors of Mortality. Legend: Initial lactate, pH, serum CO_2, and total number of vasopressors and inotropes used were significant predictors of all-cause in-hospital mortality. A decrease in pH, serum CO_2, and SVO_2 resulted in an increased hazard of mortality.

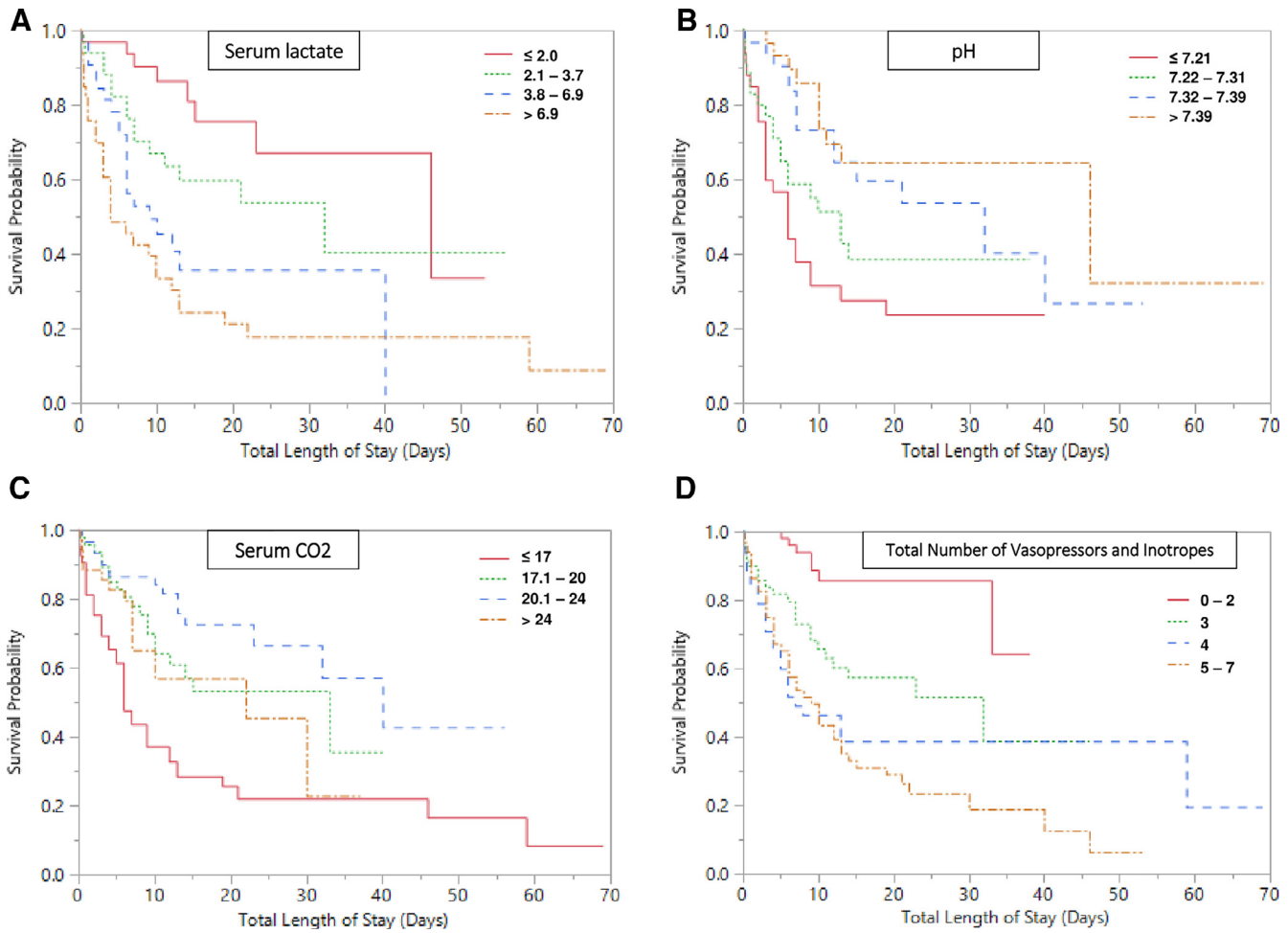

Figure 2. Kaplan-Meier survival curves of initial predictors.Survival curves of initial lactate (*A*), pH (*B*), serum CO_2 (*C*), and the total number of vasopressors and inotropes used (*D*) stratified by quartile ranges of each respective predictor.

The median survival of patients requiring 0 to 2 vasopressors and inotropes was not definable as the survival rate was >50%. Patients requiring 3 vasopressors and inotropes had a median survival of 32 days. Patients requiring 4 had a median survival of 7 days. Patients requiring 5 to 7 had a median survival of 9 days (Figure 2). A range of 0 to 7 vasopressors and inotropes was used. Mortality rate increased with increasing number of vasopressors and inotropes

(Figure 3). Figure 4 demonstrates the association of individual vasopressors and inotropes with all-cause in-hospital mortality. Norepinephrine use was associated with the highest in-hospital mortality (HR 4.26, p = 0.04, 95% CI 1.05 to 17.32). The use of epinephrine (HR 2.64, p <0.0001, 95% CI 1.73 to 4.0), vasopressin (HR 2.43, p <0.0001, 95% CI 1.60 to 3.68), phenylephrine (HR 2.09, p <0.0001, 95% CI 1.32 to 3.30), and dopamine (HR 2.23, p = 0.0003, 95% CI 1.45 to 3.44) was each independently associated with significantly increased all-cause in-hospital mortality. Milrinone (p = 0.41) and dobutamine (p = 0.36) use did not show a significant increase in mortality. Figure 5 includes a proposed guideline on determining appropriate use of the Impella in treating acute CS based on a univariate analysis of each significant initial predictor of in-hospital mortality.

Patients with the Impella >4 days had a significantly longer total hospital stay (16.4 vs 11.6 days, p = 0.03), intensive care unit stay (12.6 vs 6.9 days, p <0.001), and duration of mechanical ventilation use (7.8 vs 4.4 days, p <0.002) There was a trend toward increased mortality in patients with the Impella >4 days compared with use ≤4 days (57.8 vs 41.5%, p = 0.051).

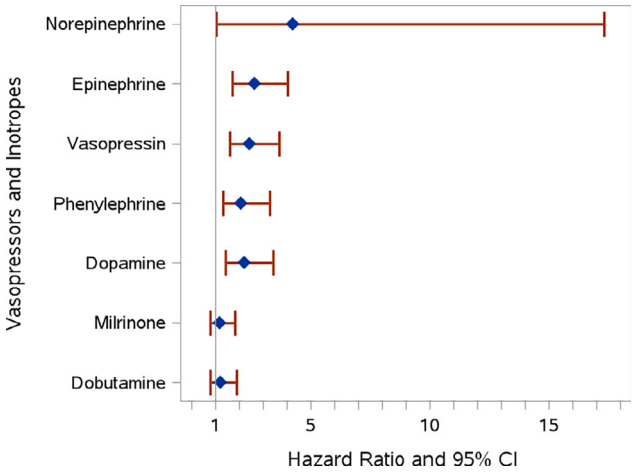

Figure 4. Individual vasopressors and inotropes and mortality. Individual hazard ratios are presented for each vasopressor and inotrope. The use of each vasopressor demonstrated a significant increase in hazard of mortality. The use of either inotrope did not show a statistically significant increase in hazard of mortality.

Discussion

Our study has the largest known series of patients to date investigating predictors of mortality in patients receiving the Impella for acute severe CS. All-cause in-hospital mortality was 45.1%, which is lower than previously reported.[11] Many studies evaluating outcomes of Impella use report 30-day mortality.[3,4,6,7,8,12,13] Evaluating in-hospital mortality is useful in determining immediate management of severe CS during index hospitalization.

The initial lactate was a strong predictor of mortality of patients treated with the Impella for acute severe CS. Nonsurvivors had an average lactate of 6.8 mmol/L before Impella implantation. The median initial lactate of all patients was 3.8 mmol/L. This data suggests that patients in CS receiving the Impella have >50% mortality with initial lactate ≥3.8 mmol/L. Hyperlactatemia is commonly used in intensive care settings, and studies have demonstrated its predictive value in patient mortality in the setting of septic shock.[14] However, clinical data on initial lactate as a predictor of mortality in patients with CS requiring the Impella remains limited. The Impella-EUROSHOCK-registry study included 120 patients who presented with CS from acute myocardial infarction receiving the Impella 2.5. The study showed that lactate ≥3.8 mmol/L at admission was a predictor of 30-day mortality. Thirty-day mortality was 64.2%.[3] Similarly, a small series of 41 patients with CS receiving the Impella identified lactate >3.8 mmol/L at admission as a predictor of 30-day mortality.[15]

Initial pH and serum CO_2 demonstrated similar trends in mortality. A pH ≤7.21 differed significantly from pH 7.32 to 7.39 and pH >7.39, highlighting significantly higher mortality with an initial pH ≤7.21. Patients with an initial

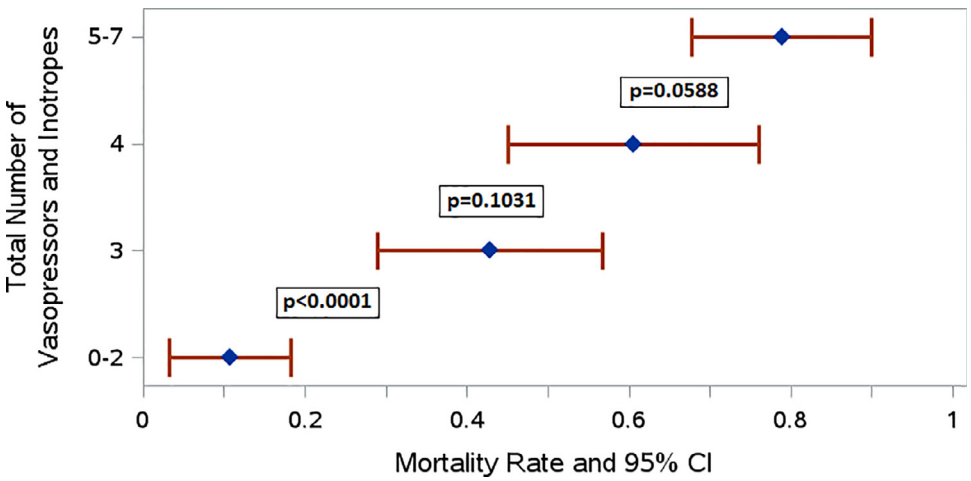

Figure 3. Total number of vasopressors and inotropes and mortality. An increase in the total number of vasopressors and inotropes used is associated with an increase in mortality. The Cochran-Armitage test is used to test for an overall linear trend in proportion of mortality across the groups (Z = 7.573, p <0.0001). The groups are then evaluated with select pairwise comparisons. A significant increase in mortality is seen with an increase from 0-2 to 3 vasopressors and inotropes (10.8% [n = 65] to 42.9% [n = 49], p <0.0001). Subsequent increases from 3 to 4 (42.9% [n = 49] to 60.5% [n = 38], p = 0.1031) and 4 to 5-7 vasopressors and inotropes (60.5% [n = 38] to 78.8% [n = 52], p = 0.0588) are not statistically significant but potentially indicative of an increase in mortality.

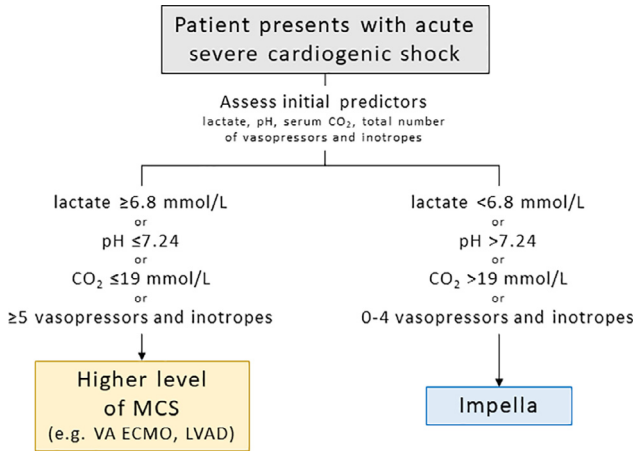

Figure 5. Impella use in acute severe cardiogenic shock. Proposed algorithm for the selection of mechanical circulatory support for patients presenting with acute severe cardiogenic shock. LVAD = left ventricular assist device; VA ECMO = venoarterial extracorporeal membrane oxygenation

serum CO_2 ≤17 mmol/L had significantly increased mortality compared with other CO_2 quartile ranges. There have been no other studies to date assessing pH or CO_2 as predictors of mortality in the setting of acute CS treated with the Impella.

Total number of vasopressors and inotropes used was the strongest predictor of mortality in our study. A prospective study of 219 patients with CS found that the use of epinephrine, norepinephrine, vasopressin, vasopressors combination, and combination of dobutamine with vasopressors were associated with increased 90-day mortality.[16] Epinephrine use was most strongly associated with 90-day mortality. Similarly in our study, none of the inotropes independently predicted mortality (Figure 4). Furthermore, the more vasopressors and inotropes used, the higher the mortality (Figure 3). This relation suggests that increasing the number of agents does not necessarily improve survival and indicates a more urgent need for escalation of care to a higher level of MCS. Another study reported increasing in-hospital mortality with an increasing vasoactive inotropic score.[17] Although neither study evaluated patients with CS with the Impella, both demonstrated the prognostic value of increasing vasopressor and inotropic support.

Our study demonstrates that a higher mortality is associated with higher initial lactate, lower initial pH, lower initial serum CO_2, and greater vasopressors and inotropes use in patients with CS treated with the Impella. The Impella may not be an appropriate level of MCS in patients with an initial lactate ≥6.8 mmol/L, initial pH ≤7.24, initial serum CO_2 ≤19.1 mmol/L, or require 5 or more vasopressors and inotropes. In such clinical scenarios, a higher level of MCS may be considered, such as venoarterial extracorporeal membrane oxygenation or an implantable left ventricular assist device (Figure 5). The cutoffs of initial predictors were derived post hoc and were significant predictors of mortality based on a univariate analysis. This algorithm could be used as a general guideline for clinicians in determining the appropriateness of the Impella in treating acute CS. However, further analyses to test for these cutoffs of initial predictors of mortality are needed.

The Impella Ventricular Support Systems received US Food and Drug Administration approval for short-term use (≤4 days for Impella 2.5 and Impella CP; ≤6 days for Impella 5.0 and Impella LD) for the treatment of CS as a result of isolated left ventricular failure.[11] No studies to date have shown improved clinical outcomes of prolonged Impella use in CS. Incidence of device complications increases with increased duration of support.[3,18,19] Prolonged Impella use increases hospital length of stay and increases hospital- and ventilator-associated complications. Prolonged Impella use showed a trend toward increased mortality, suggesting little additional survival benefit beyond 4 days of use. This finding did not reach statistical significance due to our small sample size. Although the intended use for the Impella 5.0 is up to 6 days in CS, we defined prolonged use as >4 days since most (97%) of our patients received the Impella 2.5 or Impella CP. Given the high incidence of device complications described in previous studies and prolonged hospitalization and mechanical ventilation, it is reasonable to consider escalating care to a higher level of MCS if the patient has not improved by day 4 of support with the Impella.

A major limitation of this study is its retrospective design and the small number of patients. A randomized controlled study is necessary to ascertain the role of initial biochemical parameters in predicting mortality in patients with CS receiving the Impella. A nonuniform system in evaluating patients with CS led to incomplete observations in initial biochemical values (Appendix A) which limited the ability to perform a multivariate analysis. The study population is from a single institution, which may affect generalizability of the study results.

In patients treated with the Impella for acute severe CS, initial lactate, pH, serum CO_2, and use of vasopressors and inotropes are significant predictors of all-cause in-hospital mortality. Patients with the Impella >4 days have poorer outcomes and may benefit from escalation of care. Using the initial predictors of mortality may aid in determining the appropriateness of Impella use in patients presenting with acute severe CS.

Acknowledgment

The authors thank Marsha Kadner for her assistance in collecting patient data and Jessica M. Rudd for her assistance in the initial statistical analyses.

Disclosures

The authors have no financial conflicts or funding sources to disclose. Rajnish Prasad is an advisory board member for Abiomed since 2018. WellStar Research Institute participates in clinical research trials sponsored by Abiomed. None of the authors are involved in these studies.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.05.039.

1. Goldberg RJ, Makam RC, Yarzebski J, McManus DD, Lessard D, Gore JM. Decade-long trends (2001-2011) in the incidence and hospital death rates associated with the in-hospital development of cardiogenic shock after acute myocardial infarction. *Circ Cardiovasc Qual Outcomes* 2016;9:117–125.
2. Seyfarth M, Sibbing D, Bauer I, Fröhlich G, Bott-Flügel L, Byrne R, Dirschinger J, Kastrati A, Schömig A. 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; 52:1584–1588.
3. Lauten A, Engström AE, Jung C, Empen K, Erne P, Cook S, Windecker S, Bergmann MW, Klingenberg R, Lüscher TF, Haude M, Rulands D, Butter C, Ullman B, Hellgren L, Modena MG, Pedrazzini G, Henriques JP, Figulla HR, Ferrari M. Percutaneous left-ventricular support with the Impella-2.5-assist device in acute cardiogenic shock: results of the Impella-EUROSHOCK-registry. *Circ Heart Fail* 2013;6:23–30.
4. Lemaire A, Anderson MB, Prendergast T, Stockmaster N, Goodman A, Lozane AM, Batsides G. Outcome of the Impella device for acute mechanical circulatory support. Innovations *(Phila)* 2013;8:12–16.
5. Lemaire A, Anderson MB, Lee LY, Scholz P, Prendergast T, Goodman A, Lozano AM, Spotnitz A, Batsides G. The Impella device for acute mechanical circulatory support in patients in cardiogenic shock. *Ann Thorac Surg* 2014;97:133–138.
6. Gaudard P, Mourad M, Eliet J, Zeroual N, Culas G, Rouvière P, Albat B, Colson P. Management and outcome of patients supported with Impella 5.0 for refractory cardiogenic shock. *Crit Care* 2015;19:363–374.
7. Schiller P, Vikholm P, Hellgren L. The Impella® Recover mechanical assist device in acute cardiogenic shock: a single-centre experience of 66 patients. *Interact Cardiovasc Thorac Surg* 2016;22:452–458.
8. Lackermair K, Sattler S, Huber BC, Grabmaier U, Weckbach LT, Bauer A, Theiss HD, Hausleiter J, Mehilli J, Massberg S, Brunner S. Retrospective analysis of circulatory support with the Impella CP® device in patients with therapy refractory cardiogenic shock. *Int J Cardiol* 2016 Sep;219:200–203.
9. Stretch R, Sauer CM, Yuh DD, Bonde P. National trends in the utilization of short-term mechanical circulatory support: incidence, outcomes, and cost analysis. *J Am Coll Cardiol* 2014;64:1407–1415.
10. Zuckerman BD, U.S. Food and Drug Administration. Center for Devices and Radiological Health. *Premarket Approval*: Impella Ventricular Support Systems, (PMA Number P140003). Received from: https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140003S004A.pdf.
11. Vase H, Christensen S, Christiansen A, Therkelsen CJ, Christiansen EH, Eiskjær H, Poulsen SH. The Impella CP device for acute mechanical circulatory support in refractory cardiac arrest. *Resuscitation* 2017; 112:70–74.
12. Garatti A, Colombo T, Russo C, Lanfranconi M, Milazzo F, Catena E, Bruschi G, Frigerio M, Vitali E. Left ventricular mechanical support with the Impella Recover left direct microaxial blood pump: a single-center experience. *Artif Organs* 2006;30:523–528.
13. Higgins J, Lamarche Y, Kaan A, Stevens LM, Cheung A. Microaxial devices for ventricular failure: a multicentre, population-based experience. *Can J Cardiol* 2011;27:725–730.
14. Masyuk M, Wernly B, Lichtenauer M, Franz M, Kabisch B, Muessig JM, Zimmermann G, Lauten A, Schulze PC, Hoppe UC, Kelm M, Bakker J, Jung C. Prognostic relevance of serum lactate kinetics in critically ill patients. *Intensive Care Med* 2019;45:55–61.
15. Sharma D, Gauthier S, Džavík V, Overgaard CB. Predictors of 30-day mortality and outcomes in patients who receive percutaneous left-ventricular support with an Impella assist device [abstract]. In: Transcatheter Cardiovascular Therapeutics 2015 Annual Meeting; 2015 Oct 11-15; San Francisco, CA. J Am Coll Cardiol; 2015. Abstract TCT-204.
16. Tarvasmäki T, Lassus J, Varpula M, Sionis A, Sund R, Køber L, Spinar J, Parissis J, Banaszewski M, Silva Cardoso J, Carubelli V, Di Somma S, Mebazaa A, Harjola VP, CardShock study investigators. Current real-life use of vasopressors and inotropes in cardiogenic shock - adrenaline use is associated with excess organ injury and mortality. *Crit Care* 2016;20:208–218.
17. Na SJ, Chung CR, Cho YH, Jeon K, Suh GY, Ahn JH, Carriere KC, Park TK, Lee GY, Lee JM, Song YB, Hahn JY, Choi JH, Choi SH, Gwon HC, Yang JH. Vasoactive inotropic score as a predictor of mortality in adult patients with cardiogenic shock: medical therapy versus ECMO. Rev Esp Cardiol *(Engl Ed)* 2019;72:40–47. S1885-5857(18) 30007-0.
18. Abaunza M, Kabbani LS, Nypaver T, Greenbaum A, Balraj P, Qureshi S, Alqarqaz MA, Shepard AD. Incidence and prognosis of vascular complications after percutaneous placement of left ventricular assist device. *J Vasc Surg* 2015;62:417–423.
19. Jensen PB, Kann SH, Veien KT, Møller-Helgestad OK, Dahl JS, Rud CS, Jensen MK, Jensen LO, Schmidt H, Møller JE. Single-centre experience with the Impella CP, 5.0 and RP in 109 consecutive patients with profound cardiogenic shock. *Eur Heart J Acute Cardiovasc Care* 2018;7:53–61.