



ORIGINAL RESEARCH

# Invasive Hemodynamic Monitoring in Cardiogenic Shock Is Associated With Lower In-Hospital Mortality

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**BACKGROUND:** There is increasing utilization of cardiogenic shock treatment algorithms. The cornerstone of these algorithms is the use of invasive hemodynamic monitoring (IHM). We sought to compare the in-hospital outcomes in patients who received IHM versus no IHM in a real-world contemporary database.

**METHODS AND RESULTS:** Patients with cardiogenic shock admitted during October 1, 2015 to December 31, 2018, were identified from the National Inpatient Sample. Among this group, we compared the outcomes among patients who received IHM versus no IHM. The primary end point was in-hospital mortality. Secondary end points included vascular complications, major bleeding, need for renal replacement therapy, length of stay, cost of hospitalization, and rate of utilization of left ventricular assist devices and heart transplantation. Propensity score matching was used for covariate adjustment. A total of 394 635 (IHM=62 565; no IHM=332 070) patients were included. After propensity score matching, 2 well-matched groups were compared (IHM=62 220; no IHM=62 220). The IHM group had lower in-hospital mortality (24.1% versus 30.6%,  $P<0.01$ ), higher percentages of left ventricular assist devices (4.4% versus 1.3%,  $P<0.01$ ) and heart transplantation (1.3% versus 0.7%,  $P<0.01$ ) utilization, longer length of hospitalization and higher costs. There was no difference between the 2 groups in terms of vascular complications, major bleeding, and the need for renal replacement therapy.

**CONCLUSIONS:** Among patients with cardiogenic shock, the use of IHM is associated with a reduction in in-hospital mortality and increased utilization of advanced heart failure therapies. Due to the observational nature of the current study, the results should be considered hypothesis-generating, and future prospective studies confirming these findings are needed.

**Key Words:** cardiogenic shock ■ invasive hemodynamic ■ pulmonary arterial catheter ■ Swan-Ganz catheter

Cardiogenic shock (CS) is a life-threatening condition characterized by acute end-organ hypoperfusion due to inadequate cardiac output, resulting in multi-organ failure culminating in death.<sup>1-4</sup> Contemporary data from specialized cardiogenic shock centers shows that early recognition and algorithmic approaches for managing CS with the rapid deployment of MCS are associated with a reduction in mortality.<sup>5-7</sup> Invasive hemodynamic monitoring (IHM) is the cornerstone of such treatment algorithms,

emphasizing early diagnosis and phenotyping of CS. The ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial reported a lack of benefit with IHM. Since then, there has been a decreasing trend in IHM use among patients admitted with congestive heart failure and cardiogenic shock.<sup>8-13</sup> It is essential to highlight that studies evaluating the role of IHM; including the ESCAPE trial, excluded patients with CS and were conducted before the current era of advances in

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## CLINICAL PERSPECTIVE

### What Is New?

- Among patients with cardiogenic shock, the use of invasive hemodynamic monitoring is associated with a reduction in in-hospital mortality and increased utilization of durable left ventricular assist devices and heart transplantation.

### What Are the Clinical Implications?

- The use of invasive hemodynamic data to guide the care of patients with cardiogenic shock is associated with reduced in-hospital mortality.
- Treatment protocols relying on invasive hemodynamic data in patients with cardiogenic shock should be further studied in randomized clinical trials.

## Nonstandard Abbreviations and Acronyms

<b>AHRQ</b>	Agency for Healthcare Research and Quality
<b>CS</b>	cardiogenic shock
<b>IHM</b>	invasive hemodynamic monitoring
<b>NIS</b>	National Inpatient Sample

MCS.<sup>11,14,15</sup> Using a large nationally representative sample of patients with CS, we sought to determine the impact of IHM use, as well as the timing of use, on clinical outcomes including in-hospital mortality among patients admitted with CS.

## METHODS

### Study Data

The study was derived from the National Inpatient Sample (NIS), from October 1, 2015 to December 31, 2018. The NIS database is part of the Healthcare Cost and Utilization Project (HCUP) databases and is sponsored by the Agency for Healthcare Research and Quality (AHRQ).<sup>16</sup> The NIS is the largest publicly available all-payer administrative claims-based database and contains patient discharges from 1000 hospitals in 45 states. It has clinical and resource utilization information on more than 7 million discharges annually. Weighted, it represents more than 35 million hospitalizations nationally on an annual basis. These data are stratified to represent 20% of US inpatient hospitalizations across different hospital and geographic regions (random sample).<sup>16</sup> Institutional review board approval and informed consent were not required for this study,

given the NIS database's de-identified nature and public availability. Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the Healthcare Cost and Utilization Project at [https://www.hcup-us.ahrq.gov/tech\\_assist/centdist.jsp](https://www.hcup-us.ahrq.gov/tech_assist/centdist.jsp).

### Study Population

Adult patients ( $\geq 18$  years) admitted with CS during October 1, 2015 to December 31, 2018, were identified in the NIS using the *International Classification of Disease*, Tenth Revision Clinical Modification Code (*ICD-10-CM*) R570, which was applied to all the diagnoses variables provided by the dataset. We then identified patients who underwent IHM during the same admission using the *ICD-10* procedure codes (*ICD-10-PCS*) 4A1239Z, 4A0239Z, 4A023N6, 4A023N8, 4A033J3, 4A033B3, 4A03353, 4A13353, 4A133B3, 4A133J3, and 02HP32Z, which codes for measurement, monitoring, or insertion of monitoring device to check cardiac output or pulmonary artery hemodynamics. Similar methods were used in previous studies to identify patients who received IHM.<sup>10,12,17</sup> The complete list of the codes used in the current analysis is provided in Table S1.

We excluded patients who underwent only left heart catheterization without accompanying right heart catheterization. Furthermore, we excluded the following patients: (1) patients with missing mortality, age, or sex data, (2) patients who were younger than 18 years, (3) patients who received concomitant cardiac surgery (coronary artery bypass grafting or valve surgery), transcatheter aortic valve replacement, mitral clip or catheter ablation during the same hospitalization, (4) patients who died on the day of admission, (5) patients with the diagnosis of primary pulmonary hypertension, (6) patients who were admitted electively to the hospital, and (7) patients who received the IHM after or on the same day of receiving durable left ventricular assist devices (LVADs) or heart transplantation (HT).

We have conducted several analyses on the included population as follows: (1) a primary analysis comparing the in-hospital outcomes among patients who received IHM versus no IHM, (2) a secondary analysis assessing the impact of the timing of IHM on in-hospital outcomes; this was performed by constructing 3 different matched cohorts to compare the outcomes among patients who received early IHM (eIHM) (within the first 24 hours) versus delayed IHM (dIHM) (after the first 24 hours and up to a week) and versus matched controls (no IHM), (3) sensitivity analysis by stratifying the primary outcome based on the type of the CS (acute myocardial infarction-CS [AMIC-CS or Non-AMI-CS]), (4) sensitivity analysis by restricting the

included cohort to patients who received an indwelling pulmonary artery catheter (PAC). Following methods used in previous studies, the PAC cohort was isolated by identifying patients who received codes for monitoring or insertion of monitoring device to check cardiac output or pulmonary artery hemodynamics,<sup>10</sup> and (5) sensitivity analysis by excluding patients who died within 72 hours of admission. Additionally, as previous studies suggested disparity in the management and outcomes of CS, we have conducted several subgroups analyses for the primary outcome based on demographic groups to detect heterogeneity of the treatment effect among the different subgroups as follows: (1) a subgroup analysis stratified by sex, (2) a subgroup analysis stratified by race, and (3) a subgroup analysis stratified by age.<sup>18,19</sup>

Additionally, due to the study's observational nature, we estimated the strength of unmeasured confounding using the E-Value methodology of VanderWeil and Ding.<sup>20</sup> This method estimates the minimum strength of the association that would be required between an unmeasured confounder and both exposure (IHM) and outcome (in-hospital mortality) to overcome the statistically significant effect observed in a study where residual confounding is a potential problem. The calculation was derived from the odds ratio obtained from the analysis after applying propensity score matching. Moreover, we used falsification end points analysis to further guard against residual confounders. In falsification analysis, one or more end points thought to be unrelated to the exposure of interest (IHM) are prespecified. The association between the exposure and outcome is tested after adjustment for confounders. The presence of any spurious association between the exposure and outcome suggests that the current analysis is prone to bias from unmeasured confounders.<sup>21,22</sup> For the present study, we used 2 separate falsification end points, including catheter-associated urinary tract infection and sacral decubitus ulcers.

## Study End Points

The primary end point of this study was in-hospital mortality. Secondary end points included vascular complications, major bleeding (defined as post-procedural bleeding requiring blood transfusion), need for renal replacement therapy (RRT), resources utilization surrogates (length of stay and cost of hospitalization), and utilization of advanced heart failure therapies (LVADs and HT). The need for RRT was considered to be present after excluding patients who are dialysis-dependent to isolate patients with a new requirement for RRT during the hospitalization. We also reported the percentage of patients with a concomitant code for bloodstream infection in the 2 groups as a safety end point.

## Statistical Analysis

All variables are expressed as weighted national estimates. This was done following the survey analysis method by incorporating the (HOSP\_NIS) as a clustering variable and accounting for the different strata in the NIS design using the (NIS\_STRATUM) as recommended in the AHRQ methods series.<sup>16</sup> Categorical variables were expressed as count (percentage) and compared using the Scott-Rao Chi-square test. Continuous variables were expressed as median (interquartile range) and compared using the Wilcoxon rank-sum test.

Moreover, for the primary analysis, a propensity score-matching (PSM) Model was calculated using multivariate logistic regression to derive 2 matched groups for comparative outcomes analyses (IHM versus no IHM). A nearest-neighbor 1:1 variable ratio, parallel, balanced propensity-matching model was applied using a caliper width of 0.01. The variables included in the PSM model included demographics (age, sex, and race), comorbidities (hypertension, diabetes mellitus, chronic kidney disease, chronic heart failure, peripheral vascular disease, chronic lung disease, cancer, chronic liver disease, coagulopathy, prior stroke, smoking, and obesity), clinical factors (AMI-CS or need for mechanical ventilation or percutaneous coronary intervention), MCS use, and hospital characteristics (hospital bed size and teaching status). Moreover, the same PSM model was used to derive 3 more comparative cohorts to compare the outcomes among (eIHM versus dIHM), (eIHM versus no IHM), and (dIHM versus no IHM).

Additionally, multivariable risk adjustments using several models derived from generalized structured equation modeling to account for the clustering of data within different hospitals were used to assess the impact of various confounding factors on the primary end point as follows: Model (1) adjusted for demographic and clinical comorbidities; Model (2) adjusted for demographic, comorbidities and clinical factors; Model (3) adjusted for demographic, clinical comorbidities, clinical presentation on admission, and hospital characteristics; Model (4) adjusted for demographic, clinical comorbidities, clinical presentation on admission, hospital characteristics, and MCS use; and Model (5) adjusted for demographic, clinical comorbidities, clinical presentation on admission, hospital characteristics, MCS use, and advanced heart failure therapies. Within model 5, we tested for interaction between IHM and advanced heart failure therapies. We used the cost-to-charge ratio files provided by the HCUP to convert the hospital charges to more accurate hospital costs for cost calculations. A *P* value of <0.05 was considered statistically significant. For statistical analyses, we used the statistical package for social science (SPSS) version

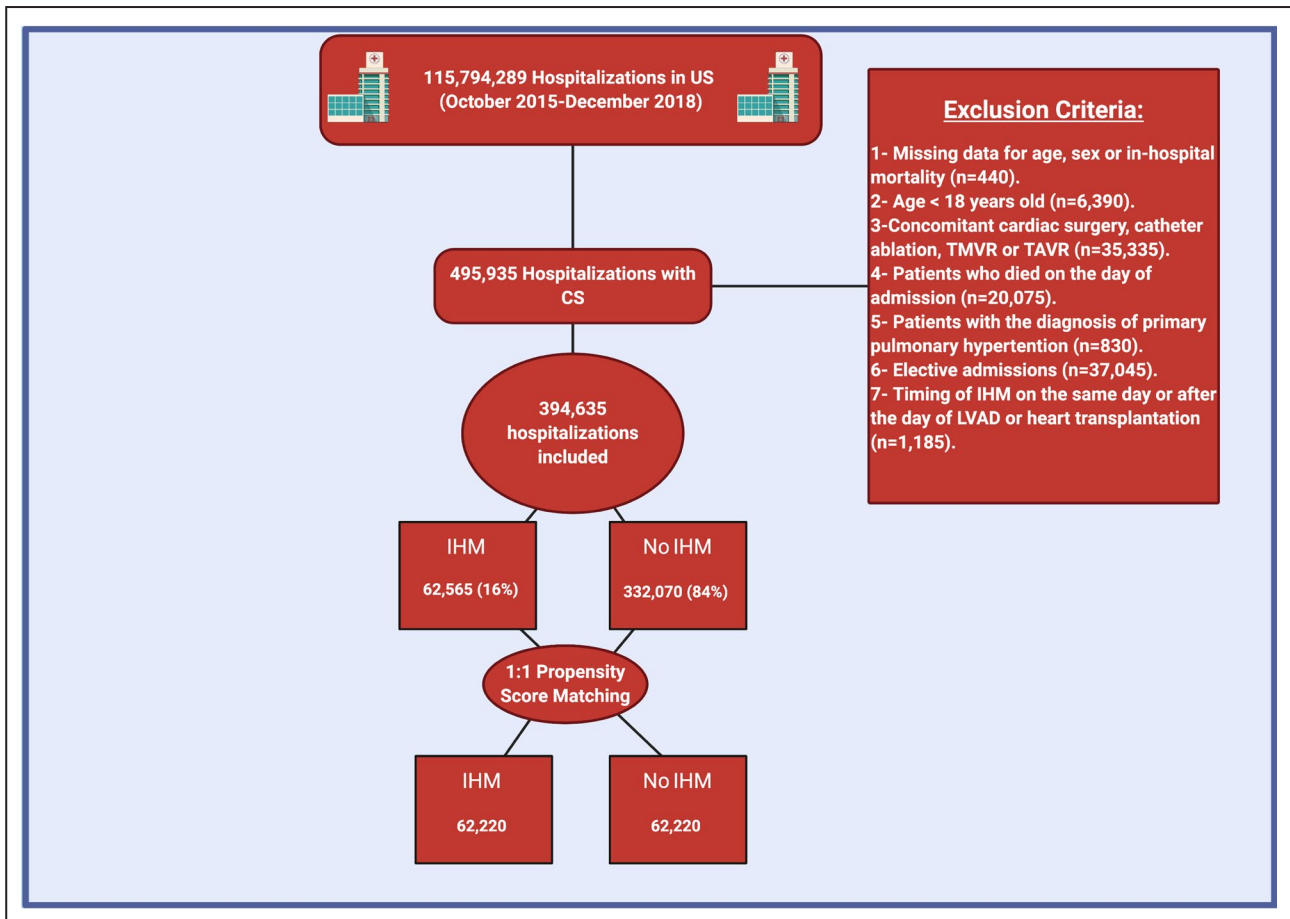
26 (IBM Corp) and R, version 3.5 for the main analysis and propensity matching, respectively. Additionally, we used Stata Statistical Software: Release 15 (Stata-Corp. 2017) to build the models for adjusted analysis using generalized structured equation modeling.

## RESULTS

A total of 394 635 (IHM=62 565; no IHM=332 070) patients qualified to be included in the current analysis. The flow chart of the study is shown in Figure 1. Comparing patients who underwent IHM to no IHM, IHM patients were younger (64 years [IQR 55–72] versus 68 years [IQR 58–78],  $P<0.01$ ), less likely to be females (33.1% versus 38.6%,  $P<0.01$ ), had higher prevalence of chronic heart failure (36.3% versus 27.9%,  $P<0.01$ ), chronic kidney disease (39.2% versus 36.8%  $P<0.01$ ), obesity (19.4% versus 17.7%,  $P<0.01$ ), and coagulopathy (25.5% versus 22.7%;  $P<0.01$ ). Moreover, the IHM had higher utilization of percutaneous coronary interventions (PCI) (23.9% versus 18.6%;  $P<0.01$ ). On the other hand, IHM patients had lower prevalence of metastatic cancer (1% versus 2.3%,  $P<0.01$ ), chronic lung

disease (24.2% versus 27.6%,  $P<0.01$ ), and prior stroke (8.3% versus 9.2%,  $P<0.01$ ). A detailed description of the baseline characteristics is shown in (Table 1).

After PSM, 2 well-matched IHM and no IHM groups were compared ( $n=62\ 220$  for each group) (Table 2). After PSM, standardized mean differences were reduced to  $<10\%$  for all the covariates, indicating a balanced population. The variables used in the PSM and the result of the PSM are shown in Figure 2. The IHM group showed lower in-hospital mortality (24.1% versus 30.6%,  $P<0.01$ , OR 0.7 [95% CI 0.67–0.74]) with higher utilization of LVADs (4.4% versus 1.3%,  $P<0.01$ ) and HT (1.3% versus 0.7%,  $P<0.01$ ) longer length of hospitalization (median=11 versus 7 days,  $P<0.01$ ) and higher costs (median=45 511\$ versus 31 290,  $P<0.01$ ). There was no difference between the 2 groups in terms of vascular complications, major bleeding, and the need for RRT (Table 2). There was a consistent reduction in in-hospital mortality in all the subgroups with no detected heterogeneity (Figure 3). Moreover, in the sensitivity analysis, the association of IHM with reduced mortality persisted in both AMI-CS (IHM=30.8% versus no IHM=34%,  $P<0.01$ ) and non-AMI-CS groups (IHM=19.4% versus



**Figure 1. Flow chart of the study.**

CS indicates cardiogenic shock; IHM, invasive hemodynamic monitoring; LVAD, left ventricular assist devices; TMVR, transcatheter mitral valve repair; and TAVR, transcatheter aortic valve replacement.

**Table 1. Baseline Characteristics of Patients Included in the Analysis Before and After Propensity Score Matching**

Variables (%)	Unmatched Cohorts			Matched Cohorts				
	IHM (n=62 565)	No IHM (n=332 070)	Total (n=394 635)	SMD	IHM (n=62 220)	No IHM (n=62 220)	Total (n=12 440)	SMD
Age, median (25th–75th IQR), y	64 (55–72)	68 (58–78)	67 (58–77)	-0.24	64 (55–73)	64 (56–75)	64 (55–74)	<0.01
Female	33.1	38.6	37.7	-0.12	33.1	32.5	32.8	<0.01
Race								<0.01
White	62	65.3	64.8		62	62.7	62.4	<0.01
Black	14.9	17.7	15.3	0.04	17.7	16.2	16.9	<0.01
Hispanic	8.4	8.8	8.7		8.4	9.4	8.9	<0.01
Other*	11	11.9	11.1		11.8	11.8	11.8	<0.01
Diabetes mellitus	40.3	39.3	39.5	0.02	40.3	40.8	40.5	<0.01
Hypertension	74.4	73.6	73.7	0.02	74.4	75	74.7	<0.01
Peripheral vascular disease	12.6	12.9	12.9	-0.03	12.6	12.4	12.5	<0.01
Chronic heart failure	36.3	27.9	29.3	0.18	36	35.7	35.9	<0.01
Chronic kidney disease	39.2	36.8	37.2	0.07	39.1	38.4	38.7	<0.01
Metastatic cancer	1	2.3	2.1	-0.14	1	1.1	1	<0.01
Coagulopathy	25.5	22.7	23.1	0.07	25.4	25.7	25.6	<0.01
Chronic liver disease	6.5	6.5	6.5	<0.01	6.4	6.1	6.3	<0.01
Chronic lung disease	24.2	27.6	27.1	-0.09	24.3	24.9	24.6	<0.01
Obesity	19.4	17.7	17.9	0.04	19.4	19.9	19.6	-0.02
Prior stroke	8.3	9.2	9	-0.03	8.3	8.1	8.2	0.01
Smoking	15.2	16.5	16.3	-0.05	15.2	15.1	15.2	<0.01
STEMI	19.8	20.2	20.1	-0.04	19.9	20.3	20.1	-0.02
NSTEMI	21.9	22.5	22.4	-0.05	21.9	22.2	22	-0.01
Mechanical ventilation	39.7	49.1	47.6	-0.21	39.9	39.8	39.8	0.02
PCI	23.9	18.6	19.5	0.1	23.8	24	23.9	-0.01
ECMO	3.7	2	2.2	0.09	3.6	3.5	3.5	<0.01
Impella®	17.3	15.2	15.5	0.06	17.2	18	17.6	<0.01
IABP	23.7	11.6	13.5	0.27	23.3	22.7	23	<0.01
Hospital bed size								
Small	7.2	13.9	12.9	0.37	7.2	6.5	6.9	<0.01
Medium	18.8	27.1	25.8		18.9	19.9	19.4	
Large	74	59	61.4		73.9	73.6	73.7	
Hospital teaching status								
Rural non-teaching	1.9	4.5	4.1	0.39	7.2	6.5	6.9	0.03
Urban non-teaching	10.6	20.5	18.9		18.9	19.9	19.4	
Urban teaching	87.5	75	77		73.9	73.6	73.7	

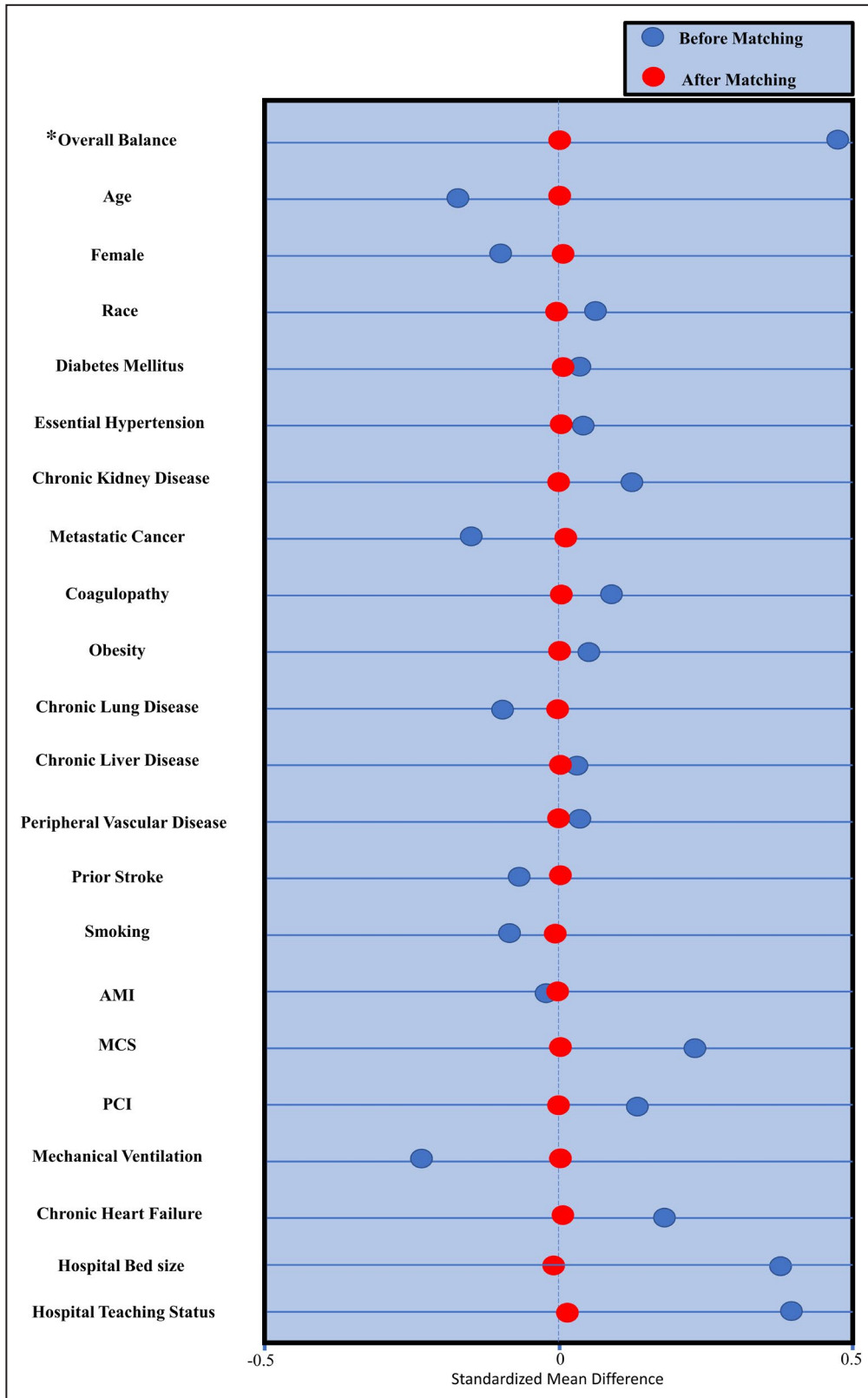
ECMO, extra-corporeal membrane oxygenation; IABP indicates intra-aortic balloon pump; IHM, invasive hemodynamic monitoring; IQR, inter-quartile range; SMD, standardized mean difference; NSTEMI, non-ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, non–ST-segment–elevation myocardial infarction.  
 \*Other includes Asian or Pacific Islander, Native American and unknown race.



**Table 2. In-Hospital Outcomes of Patients Included in the Analysis Before and After Propensity Score Matching**

Variables no. (%)	Unmatched cohorts			Matched cohorts			P value	Total (n=12 440)	P value
	IHM (n=62 565)	No IHM (n=332 070)	Total (n=394 635)	IHM (n=62 220)	No IHM (n=62 220)	Total (n=12 440)			
<b>In-hospital outcomes</b>									
Death	24.1	35.8	34	24.1	30.6	27.4	<0.01		<0.01
Vascular complications	0.9	0.7	0.7	0.9	0.9	0.9	0.01		0.89
Major bleeding	4.9	4.9	4.9	4.8	5.4	5.1	0.77		0.06
RRT	9.4	8.7	8.8	9.4	9	9.2	0.02		0.24
Central line associated bloodstream infections	0.6	0.4	0.4	0.6	0.4	0.5	<0.01		<0.01
<b>Utilization of advanced heart failure therapy</b>									
LVAD	4.5	0.6	1.2	4.4	1.3	2.8	<0.01		<0.01
Heart transplantation	1.4	0.3	0.5	1.3	0.7	1	<0.01		<0.01
<b>Resources utilization</b>									
Length of hospitalization median days (25th–75th IQR)	11 (6 – 19)	7 (3 – 13)	7 (3 – 14)	11 (6 – 18)	7 (4 – 14)	9 (5 – 16)	<0.01		<0.01
Cost of hospitalization median \$ (25th–75th IQR)	46 553 (25 685–87 062)	28 117 (14 848–51 918)	30 607 (16 129–57 055)	45 511 (25 809–81 470)	31 290 (16 364–58 325)	38 098 (20 579–69 981)	<0.01		<0.01

IHM indicates invasive hemodynamic monitoring; IQR indicates inter-quartile range; LVAD, left ventricular assist devices; and RRT, renal replacement therapy.



**Figure 2.** Dot plot showing covariates balance before and after the propensity matching. AMI indicates acute myocardial infarction; MCS, mechanical circulatory support; and PCI, percutaneous coronary intervention. \*Overall balance represents the average standardized mean difference for all the covariates before and after the propensity score matching.

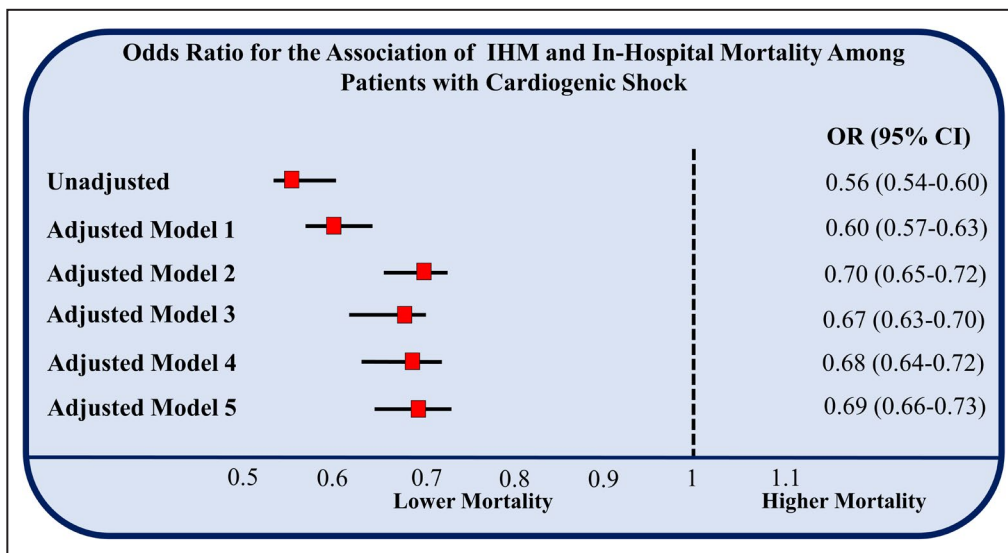
Subgroups	OR (95% CI)	p for Interaction
<b>❖ Sex</b>		
• Female	0.70 (0.64-0.77)	0.80
• Male	0.72 (0.67-0.78)	
<b>❖ Age (years)</b>		
• < 65	0.66 (0.62-0.73)	0.12
• ≥ 65	0.75 (0.70-0.81)	
<b>❖ Race</b>		
• Caucasians	0.75 (0.69-0.80)	0.64
• Non-caucasians	0.67 (0.60-0.74)	

Favors IHM
1
Favors No IHM

**Figure 3. Result from the subgroup analysis.**  
 IHM indicates invasive hemodynamic monitoring; and OR, odds ratio.

no IHM 37.4%,  $P < 0.01$ ). Additionally, in the sensitivity analyses in which patients who died within 72 hours were excluded or the analysis was restricted to the PAC cohort, the association of IHM with reduced in-hospital mortality remained statistically significant (IHM=18.1%, no IHM=20%,  $P < 0.01$ ) and (PAC=28%, no PAC=31%,  $P = 0.02$ ), respectively. The IHM group had a higher percentage of bloodstream infection than the no IHM group (0.6% versus 0.4%,  $P < 0.01$ ).

In the risk-adjusted analyses, the use of IHM continued to be associated with lower in-hospital mortality. In model 1, adjusting for demographics and comorbidities, the utilization of IHM was associated with reduced in-hospital mortality (adjusted odds ratio [aOR] 0.60, 95% CI 0.57–0.63). The results were consistent in model 2, which also adjusted for clinical factors present on admission (aOR 0.70, 95% CI 0.65–0.72), in model 3, which additionally adjusted for hospital



**Figure 4. Results of the multivariable risk adjustment analysis**  
 IHM indicates invasive hemodynamic monitoring; and OR, odds ratio.



characteristics (aOR 0.67, 95% CI 0.63–0.70), in model 4, which additionally adjusted for temporary MCS (aOR 0.68, 95% CI 0.64–0.72), and in model 5, which was the most robust Model which included all the previously mentioned covariates and additionally adjusted for the use of advanced heart failure therapy (aOR 0.69, 95% CI 0.66–0.73) (Figure 4). The utilization of IHM was associated with reduced in-hospital mortality regardless of the utilization of advanced heart failure therapies ( $P$  for interaction=0.86).

In an additional analysis comparing the timing of IHM, both early and delayed IHM were associated with better in-hospital mortality compared to no IHM (eIHM=26% versus no IHM=30%,  $P<0.01$ ) and (dIHM=21.5% versus no IHM=29%,  $P<0.01$ ), respectively. However, after PSM comparing early versus delayed IHM, there was no difference between the 2 in terms of in-hospital mortality (eIHM=22.2% versus dIHM=22.7%,  $P=0.61$ ) (Table 3).

To quantify the strength of any possible unmeasured confounder, we calculated the E-Value following the methodology of VanderWheeler and Ding for the primary outcome of in-hospital mortality.<sup>20</sup> The E-Value (Odds Ratio Scale) for in-hospital mortality was 1.7. Thus, our observed reduction in in-hospital mortality among patients who were admitted with CS and treated with IHM could potentially be explained by an unmeasured confounder that was associated with both the use of IHM and reduction of in-hospital

mortality by an OR of 1.7, but weaker confounders could not explain this association. Moreover, while the primary analysis showed an association between IHM use and reduced in-hospital mortality, there was no statistical evidence of a spurious association between IHM and any of the falsification end points used in the current study as follow: catheter-associated urinary tract infection (IHM=0.3%, no IHM=0.3%,  $P=0.9$ ) and sacral ulcers (IHM=2.62%, no IHM=2.6%,  $P=0.1$ ).

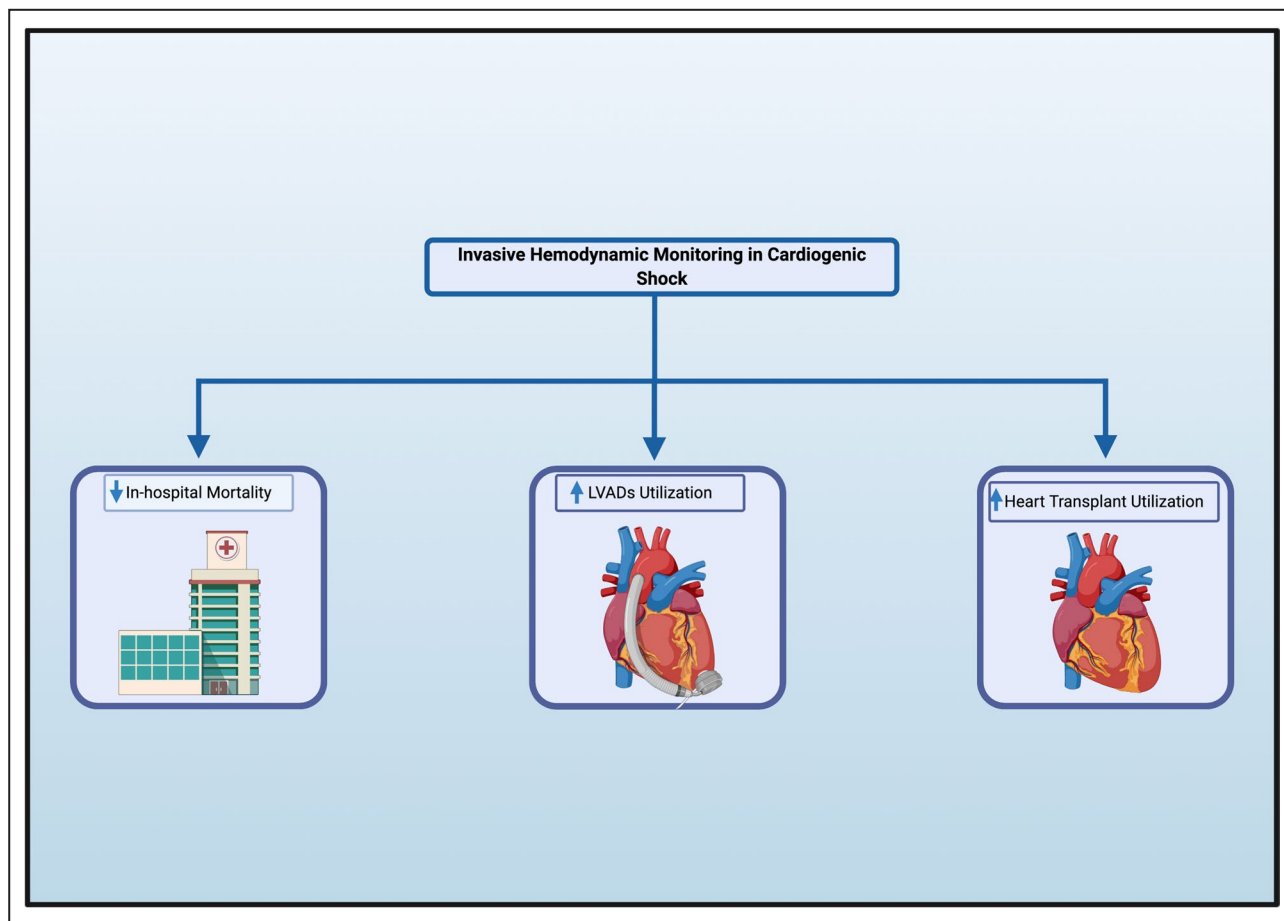
## DISCUSSION

This is the largest contemporary study, using a nationally representative sample of patients with CS, assessing the impact of IHM on clinical outcomes. There are several significant findings from our study as follow: (1) Among all hospitalized patients with CS, IHM is associated with a significant reduction in in-hospital mortality, (2) the use of IHM is associated with higher utilization of advanced heart failure therapies (LVADs and HT), (3) IHM is associated with reduced mortality in CS for both AMI-CS and non-AMI-CS, (4) the association between use of IHM and reduced in-hospital mortality was consistent among the different subgroups (males versus females, White versus non-White, and old versus young patients) (Figure 5), (5) the IHM group was associated with longer length of stay and higher cost compared to the no IHM group, and (6) the IHM group

**Table 3. In-Hospital Outcomes Based on Timing of IHM of the Patients Included in Analysis Before and After Propensity Score Matching**

Variables no. (%)	Unmatched cohorts				Matched cohorts			
	Early IHM (n=30 430)	Late IHM (n=21 145)	Total (n=51 575)	P Value	Early IHM (n=17 735)	Late IHM (n=17 735)	Total (n=35 470)	P Value
In-hospital outcomes								
Death	26.9	21.5	24.7	<0.01	22.2	22.7	22.4	0.61
RRT	8	9.3	8.5	<0.01	8.6	9.2	8.9	0.33
Heart transplant	0.6	1.3	0.9	<0.01	1	1.3	1.1	0.17
LVADs	3.2	5.2	4	<0.01	4.6	4.8	4.7	0.77
	Early IHM (n=30 430)	No IHM (n=332 070)	Total (n=362 500)	P Value	Early IHM (n=30 340)	No IHM (n=30 340)	Total (n=60 680)	P Value
Death	26.9	35.4	34.7	<0.01	26	30	28	<0.01
RRT	8	8.9	8.8	0.044	8	8.5	8.2	0.36
Heart transplant	0.6	0.5	0.5	0.17	0.6	0.9	0.7	0.052
LVADs	3.2	0.8	1	<0.01	3.2	1.3	2.2	<0.01
	Late IHM (n=21 145)	No IHM (n=332 070)	Total (n=353 215)	P Value	Late IHM (n=21 025)	No IHM (n=21 025)	Total (n=42 050)	P Value
Death	22	35	34.5	<0.01	21.5	29	25.3	<0.01
RRT	9.3	8.9	8.9	0.34	9.3	10	9.6	0.28
Heart transplant	1.3	0.5	0.5	<0.01	1.2	1.3	1.2	0.63
LVADs	5.2	0.8	1.1	<0.01	5.1	2.3	3.7	<0.01

IHM indicates invasive hemodynamic monitoring; LVAD, left ventricular assist devices; and RRT, renal replacement therapy.



**Figure 5. Summary of the main findings from the study.**

Arrows indicate reduction in in-hospital mortality and higher left ventricular assist devices (LVADs) utilization and heart transplant utilization.

had a higher percentage of concomitant bloodstream infections compared to the no IHM group.

Literature supporting hemodynamic monitoring in CS dates as far back as the 1970s.<sup>23</sup> Data from the SHOCK registry from  $\approx 2$  decades back showed that IHM in CS provides prognostic information that predicts mortality.<sup>24</sup> Contemporary literature from the cardiogenic shock working group indicates that IHM can be used for phenotyping CS (left ventricular shock, right ventricular shock, or biventricular shock) and guide initial triaging, as well as directing timely escalation of pharmacologic or mechanical support in CS.<sup>25-28</sup> A recent study utilized NIS data from 2000 to 2014; the authors reported a 75% reduction in IHM over the study period and found no reduction in in-hospital mortality in the IHM group.<sup>10</sup> The differences in the findings between our study and the previous analysis can be explained by several means. First, our analysis included more contemporary data extending from October 2015 until December 2018. During the study period, there have been advances in the care of patients with CS after adopting CS treatment algorithms on a national scale.<sup>5-7</sup> Secondly, the previous study included only

patients with AMI-CS. In contrast, in the current analysis, we included all CS types and performed a sensitivity analysis based on CS type. In another study, Hernandez et al specifically studied the role of IHM among patients admitted with acute decompensated heart failure (ADHF). They showed higher mortality with the use of IHM in patients with ADHF without CS.<sup>8</sup> Among patients with CS, IHM's use was associated with lower mortality, consistent with our findings.<sup>8</sup> Moreover, smaller studies from specialized CS centers showed that the use of IHM among patients with AMI-CS is associated with improved survival.<sup>5,6</sup>

Although an association was observed between IHM use in CS and reduced mortality, this does not imply causality. The IHM-derived invasive hemodynamic monitoring provides essential diagnostic and prognostic data. It requires that this data be interpreted accurately and coupled with an expeditious and appropriate treatment strategy to improve clinical outcomes.<sup>2,29</sup> Sionis et al, in a study from a European multi-center registry of patients with CS, showed that patients who received IHM were managed more aggressively, including more frequent use of vasopressors, inotropes, and mechanical assist

devices.<sup>30</sup> We hypothesize that improvement in survival with IHM use in CS is due to earlier recognition, phenotyping, and appropriate triaging of patients with CS. This approach encourages tailored therapeutic interventions directed at the preservation of end-organ function and myocardial recovery. Using this strategy of IHM coupled with appropriate, timely use of MCS, specialized CS centers have shown a dramatic reduction in mortality in CS.<sup>5,6,7,25</sup> Moreover, consensus documents have also endorsed the routine early use of IHM among all patients with CS.<sup>2,29</sup>

Our analysis showed an association between IHM use in CS and higher LVAD and HT utilization. In contemporary practice, patients with CS are often stabilized with temporary MCS, and appropriate candidates are bridged to definitive advanced therapies including durable LVAD or HT.<sup>31</sup> Early recognition of evolving CS, allowing for interventions aimed to preserve or improve failing end-organ function, are paramount in maintaining physiologic candidacy for definitive advanced therapies. Without prompt interventions, multi-organ failure may ensue, rendering patients with CS no longer candidates for advanced therapies. Furthermore, IHM informed CS phenotyping helps guide selective bridging strategies to definitive therapy.<sup>31</sup> For instance, an essential benefit of IHM is early recognition of biventricular failure, which is often under-recognized and may warrant consideration of bi-ventricular support.<sup>26</sup>

It is important to note that the current analysis was limited to only 3 months of data reflecting the current United Network for Organ Sharing (UNOS) HT allocation scheme (implemented in September 2018). The updated UNOS allocation scheme has shifted priority from patients supported with durable devices to those with temporary mechanical support. A future study incorporating more data in the updated UNOS HT allocation scheme will be of interest.

In the contemporary era of robust MCS availability, early recognition of CS and IHM-guided therapy is critical to prevent progression from hemodynamic insufficiency to profound hemo-metabolic derangement, which is invariably associated with higher mortality.<sup>32</sup> Hemodynamic data provided by IHM can confirm evolving CS and provide vital information used to customize a therapeutic strategy based on severity and phenotype. Moreover, IHM provides real-time feedback about adequacy of therapy and to determine if escalation in pharmacologic or mechanical support is warranted.<sup>26,29,32</sup>

## Study Limitations

Our study has several limitations that need to be considered when interpreting the result from the current analysis. First, this is a retrospective observational study that is prone to unmeasured confounding variables.

However, we addressed the unmeasured confounding risk by using PSM, conducting several sensitivity analyses, and calculating the strength of the unmeasured confounder needed to change the study results (E-Value). Second, this analysis uses billing codes to identify procedures and outcomes, and those are subject to under- or over-coding. However, we used a hard clinical end point for the primary outcome (death), which is less prone to coding errors. Third, due to the dataset's inherent limitation, we do not have hemodynamic, metabolic, or clinical data, which is vital in staging cardiogenic shock. There is emerging data that the efficacy of various therapeutic interventions depends on the stage of CS.<sup>28</sup> Fourth, the current analysis is prone to survivor treatment selection bias. It is likely that the sickest patients in extremis (Stage E CS), who have the highest mortality, receive fewer diagnostic maneuvers like IHM. However, we have accounted for that by excluding the patients with severe cardiogenic shock who died within 24 hours of admission, thus increasing the validity of our study. Furthermore, we performed an additional sensitivity analysis excluding patients who died within 72 hours from admission to reduce the chance of survivor treatment bias. Fifth, the NIS database does not provide data on the hospital unit (medical intensive care versus cardiac intensive care or a step-down unit) and hence could not control for that in the current analysis. The IHM group may be a marker for admission to cardiac intensive care units, which are linked to better outcomes, including in-hospital mortality among patients with CS.<sup>33</sup> Sixth, due to the NIS sampling change after the year 2011, it is no longer possible to conduct hospital volume analysis. Consequently, we were not able to adjust for that in the current analysis. However, we have used hospital bed size and teaching status as surrogates for hospital volume. Seventh, although we report an association between IHM and utilization of advanced heart failure therapies, it is well known that right heart catheterization is a crucial part of the workup for patients who are undergoing elective HT or LVAD. However, we excluded patients who were admitted electively or patients who received the IHM after or on the same day of receiving LVAD or HT. It is essential to note that the current observational nature of the analysis makes it hypothesis-generating. The conclusions from the current analysis draw attention to the need for further prospective studies to confirm the association between IHM use and improved in-hospital mortality among patients with CS.

## CONCLUSIONS

Among patients admitted with CS, we observed an association between IHM utilization and reduced in-hospital mortality. Moreover, IHM was associated with

higher utilization of advanced heart failure therapies (LVADs and HT). The findings suggest that a hemodynamic guided approach to CS management may improve survival. Due to the observational nature of the current study, the results should be considered hypothesis-generating, and future prospective studies confirming these findings are needed.

## ARTICLE INFORMATION

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### Supplementary Material

Table S1

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# **SUPPLEMENTAL MATERIAL**



**Table S1. International classification of disease-10<sup>th</sup> modification codes Used in the Analysis**

Disease/ Complication	Codes
<b>ACS</b>	I210, I2101, I2102 , I2109, I211 , I2111 , I2119 , I212 , I2121 , I2129 , I213 , I214 , I219
<b>Comorbidities</b>	Elixhauser Comorbidity Codes
<b>Percutaneous coronary intervention</b>	0270346,027034Z,0270356,027035Z,0270366,027036Z,0270376,027037Z,02703D6,02703DZ,0272346,027234Z,0272356,027235Z,027236Z,02703EZ,0272366,0272376,027237Z,02723D6,02723DZ,02703E6,02703F6,02703FZ,02703G6,02703GZ,02703Z6,02703ZZ,0270446,027044Z,0270456,02723E6,02723EZ,02723F6,02723FZ,02723G6,0272446,027045Z,0270466,027046Z,0270476,027047Z,02704D6,02723GZ,02723Z6,02723ZZ,027244Z,0272456,02704DZ,02704E6,02704EZ,02704F6,027245Z,0272466,027246Z,0272476,027247Z,027247Z,02724D6,02724DZ,02724E6,02724EZ,02724F6,02704FZ,02704G6,02704GZ,0271346,027134Z,0271356,027135Z,0271366,027136Z,02704Z6,02704ZZ,02724FZ,02724G6,02724GZ,02724Z6,02724ZZ,0273346,027334Z,0273356,027335Z,0273366,027336Z,0271376,027137Z,02713D6,02713DZ,02713E6,02713EZ,02713F6,02713FZ,02713G6,02713GZ,02713Z6,0273376,027337Z,02733D6,02733DZ,02733E6,02733EZ,02733F6,02733FZ,02733G6,02733GZ,02733Z6,02713ZZ,0271446,027144Z,0271456,027145Z,0271466,027146Z,0271476,027147Z,02733ZZ,0273446,027344Z,0273456,027345Z,0273466,027346Z,0273476,027347Z,02714D6,02714DZ,02714E6,02714EZ,02714F6,02714FZ,02714G6,02714GZ,02714ZZ,02714Z6,02734D6,02734DZ,02734E6,02734EZ,02734F6,02734FZ,02734G6,02734GZ,02734Z6,02734ZZ.
<b>Vascular complications</b>	S36899A,T81718A,T81719A,T8172XA,T81710A,T81711A,T801XXA,I770,S2500XA,S2501XA,S2502XA,S2509XA,S3500XA,S3501XA,S3502XA,S3509XA,S75011A,S75012A,S75019A,S75021A,S75022A,S75029A,S75099A,I97410,I97411,I97418,I9742,I97610,I97611,I97618,I97620,L7602,L7622,M96811,M96831,I9751,I9752,L7612,M96821,T8171,T8172,S25499A,S3559XA,S45001A,S45099A,S75001A,S75199A,S85001A,S85599A
<b>Post-procedural bleeding</b>	I97410,I97418,I97610,I97618,I97630,I9742,I97620,I97410,I97411,I97418,I9742,I97610,I97621,I97630,I97640,I97618,I97621,L7602,L7622,M9681,M9683,M96811,K661,D62
<b>Blood transfusion</b>	30233M*,30233N*,30233P*,30233R*,30233T*,30233V*,30233W*,30233W*,30233W*,30233W*,30240H*,30240J*,30240K*,30240L*,30240M*,30240N*,30240P*,30240R*,30240T*,30240V*,30240W*,30240T*,30243H*,30243K*,30243L*,30243H*,30243M*,30243N*,30243P*,30243R*,30243T*,30243V*,30243W* ,3028***
<b>Renal Replacement Therapy</b>	5A1D70Z, 5A1D80Z, 5A1D90Z, 5A1D60Z, 5A1D00Z
<b>Left Ventricular Assist Device</b>	02HA0QZ
<b>Heart Transplant</b>	02YA0Z0, 02YA0Z1
<b>ECMO</b>	5A1522F, 5A1522G, 5A15A2F, 5A15A2G, 5A15223
<b>Impella ® pumps</b>	5A0221D, 5A0211D
<b>IABP</b>	5A02210