

Characteristics and Outcomes of Patients With Cardiogenic Shock Utilizing Hemodialysis for Acute Kidney Injury



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In the setting of cardiogenic shock (CS), impaired biventricular function can cause acute decrease in renal function via reduced renal perfusion and increased renal venous pressure. We sought to analyze the characteristics and outcomes of patients hospitalized with CS who utilized renal replacement therapy (hemodialysis) for acute kidney injury (AKI-HD). We utilized data from the National Inpatient Sample to calculate national rates of in-hospital mortality, use of temporary mechanical support, vascular injury requiring surgery, length of stay (LOS) and hospitalization cost from 2010 to September 2015. We compared the in-hospital outcomes between CS with AKI-HD and a propensity score-matched group without AKI-HD. We identified 6,076 hospitalizations (weighted n = 24,272) with CS and AKI-HD and 76,878 (weighted n = 378,553) with CS not AKI-HD. Among these cases 48.1% (n = 39,403, weighted n = 193,746) had ST elevation myocardial infarction as the cause of CS. Patients with CS and AKI-HD had higher comorbidity burden and they were also more likely to receive mechanical circulatory support device (absolute standardized difference >10% for all comparisons) compared with CS patients without AKI-HD. After matching 4,457 cases for patient-level and hospital-level characteristics, CS with AKI-HD was associated with significantly higher in-hospital mortality (75.74% vs 51.58%, p <0.001), use of temporary mechanical support (24.0% vs 19.3%, p <0.001), LOS (21.4 vs 14.4 days, p <0.001) and cost (\$80,406 vs \$52,833, p <0.0001). AKI-HD occurred in approximately 6% of patients with CS in years 2010 to 2015 and was associated with significantly increased in-hospital morbidity and mortality, LOS, and cost. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1816–1821)

The kidney is remarkably sensitive to decreased perfusion. In the setting of CS, impaired biventricular function can cause acute decrease in renal function and acute kidney injury (AKI) via reduced renal perfusion and increased renal venous pressure. Unsurprisingly, in the setting of CS, worsening renal function is not only a sign of inadequate end-organ perfusion, but also a crucial prognostic indicator of short-term mortality.¹ Although current evidence indicates that development of AKI in CS connotes poor prognosis, the clinical and prognostic implications of renal replacement therapies and specifically hemodialysis (HD) in this clinical setting remain poorly defined. HD improves renal function and rectifies electrolyte derangements; it remains unclear if HD offers mortality benefits in the setting of cardiogenic shock.

With this analysis, we sought a unique opportunity to examine the characteristics of patients hospitalized with CS who utilized hemodialysis for acute kidney injury (AKI-HD) and its clinical consequences using a large, nationally representative database.

Method

The study was conducted utilizing the National Inpatient Sample (NIS) database which is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by Agency for Healthcare Research and Quality.² NIS is the largest all-payer inpatient stays database in the United States. It represents a 20% stratified sample of all discharges from community hospitals in the United States excluding rehabilitation and long-term acute care hospitals. NIS data were queried using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) to identify the study variables. All adult patients (age ≥18 years) with cardiogenic shock using International Classification of Diseases, 9th Revision (ICD-9) diagnostic code of 785.51 between January 2010 and September 2015 were included in the study analysis. We excluded patients who were transferred between facilities or had pre-existing or know history of end stage renal disease. Patients who developed AKI who had HD were identified using ICD 9 CM codes ([Supplemental table](#)).

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We compared baseline characteristics, mortality, hospital outcomes, length of stay, and cost of hospitalization in those with or without AKI with HD. The primary outcome was all-cause in-hospital mortality. Secondary outcomes were the in-hospital complications, use of mechanical circulatory support, and assessment of healthcare resources was performed by comparing hospitalization cost and length of stay. To calculate the estimated cost of hospitalization, the NIS data was merged with cost-to-charge ratios available from the HCUP. We estimated the cost of each inpatient stay by multiplying the total hospital charge with cost-to-charge ratios. Adjusted cost for each year was calculated in terms of the 2017 cost, after adjusting for inflation according to the latest consumer price index data.³

To account for demographic factors, we included race (Whites, Non-Hispanic Blacks, Hispanics Asians, and Others), gender (female and male), health insurance type (Medicare, Medicaid, Private, Self-pay, and Others), and income level based on the zip code (lowest quartile, second quartile, third quartile, and highest quartile). We also included variables for hospital-level factors: region (Northeast, Midwest, South, and West), and hospital size (small, medium, and large sizes). The comorbidities were identified using the Agency for Healthcare Research and Quality comorbidity measures. The severity of comorbidities was identified using the Elixhauser comorbidity index.⁴

The data extraction and analysis were done with Statistical Analysis System (SAS V.9.4, SAS Institute Inc., Cary, North Carolina). To compare the baseline characteristics, we used absolute standardized differences (ASD). ASD (calculated as the differences in means or proportions divided by a pooled estimated of the SD) is not as sensitive to sample size compared with traditional significance testing and hence, useful in identifying clinically meaningful differences. An ASD of >0.1 is considered clinically meaningful.⁵ We chose a *p* value of <0.05, reported the effect sizes, 95% confidence intervals (CI), and *p* values for outcome variable comparison.

Propensity score (PS) matching model was developed to reduce the effect of selection bias and to derive 2 matched groups for comparative outcomes analysis.⁶ The PS was calculated using multivariable logistic models derived from hospitals level, demographic covariates, and comorbidities. We performed matching on the PS implementing a greedy algorithm to construct a balanced match of CS patients with AKI-HD cases to those without AKI-HD cases in a 1:1 ratio using a caliper of 0.1. We identified 4,457 (unweighted) patients in each group after the PS matching. After performing the PS matching, we checked the balance of the baseline characteristic between the 2 groups. A balance of >10% of the standardized difference between the 2 groups was considered significant.⁷ Matching achieved similar baseline characteristics between the 2 groups (Table 2).

We evaluated the trend in mortality by fitting a Poisson regression model with a robust error variance to evaluate for changes in mortality per year and adjusting for demographic, comorbidities, and hospital characteristic while inserting “year” as a continuous variable and assuming a linear association. Multivariate logistic regression models were built to determine the factors associated with AKI-HD.

We excluded all the missing variables from the analysis, and therefore, did a complete case analysis. Binary outcomes (in-patient mortality, bleeding requiring transfusion, and mechanical circulatory support use) were modeled with binomial logistic regressions. The non-normal numeric (skewed) distributions of length of stay and hospitalization cost were transformed by a natural logarithmic scale and back-transformed to obtain the expected numeric values. They were modeled with generalized linear regressions, accounting for the matching, and with a negative binomial function and gamma function, respectively. We reported odds ratio (OR) for our binary outcome, and mean ratios for the numeric outcomes. As recommended by HCUP, analyses were performed in SAS with appropriate statements to account for the complex clustered sampling methodology.^{8,9}

Results

The demographic and clinical characteristics are presented in Table 1. From January 2010 to September 2015, we identified estimated 402,825 hospitalizations with CS. Patients with AKI-HD were 24,272 (6.03%) of all discharges (supplemental figure 1). Among these cases 48.1% (*n* = 39,403, weighted *n* = 193,746) had ST elevation myocardial infarction as the cause of CS. Hospitalized patients with CS were predominantly male and White. A large proportion of the patients were admitted at urban teaching hospitals, had multiple comorbidities with Elixhauser index ≥ 4 , and most likely mechanical circulatory support device use was IABP. Compared with non-AKI-HD, patients with AKI-HD were more likely younger (mean age, 63.83 vs 66.17 years; ASD = 16.94%) and black (16.78% vs 13.00% ASD = 15.56%). Although, they were less likely to smoke and have history of dyslipidemia, a larger proportion of AKI-HD patients than non-AKI-HD had diabetes mellitus, atrial fibrillation, obesity, congestive heart failure, chronic liver disease, and chronic renal failure. They are also more likely to be hospitalized in urban, teaching hospitals and more likely to receive ECMO device (ASD >10% for all comparisons) (Table 1).

After PS matching, 4,457 patients with CS who utilized HD were compared with 4,457 patients with CS that did not utilize HD. The baseline characteristics did not differ significantly between groups as suggested by absolute standardized difference of <10% for all baseline variables (Table 2). After PS matching, compared with patients without AKI-HD, those who had AKI-HD experienced approximately 3-fold increased odds of in-hospital mortality (71.74% vs 51.20%; OR, 2.98; 95% CI, 2.73–3.26). Also, they were at significantly increased odds of T-MCS (23.99% vs 19.27%; OR, 1.32; 95% CI, 1.19–1.46). Bleeding requiring transfusion was higher in patients with AKI-HD. Among patients surviving to discharge, those with AKI-HD were less likely to be discharged home. Health care resource was increased in AKI-HD cohorts with significantly higher cost (\$80,406,163 vs \$52,833, *p* <0.0001). Among those who survived till hospital discharge, the AKI-HD cohort had longer hospital stay (mean 21.35 days vs 14.38 days, *p* <0.0001) (Table 3). We did not observe significant changes in the mortality

Table 1
Baseline characteristics of participants with cardiogenic shock by acute kidney injury requiring dialysis—unmatched

Variables	Acute kidney injury requiring dialysis			¥ASD
	No	Yes	Total	
No. of observation, unweighted	76,878	4,930	81,808	
No. of observation, weighted	378,553	24,272	402,825	
Age—year, mean (SD)	66.33(14.88)	63.83(14.62)	66.17(18.00)	16.94
Women	38.06%	34.58%	37.85%	7.41
				15.56
- White	71.98%	65.06%	71.56%	
- Black	12.76%	16.78%	13.00%	
- Hispanic	7.86%	9.32%	3.06%	
- Asia	3.00%	4.01%	4.43%	
Dyslipidemia	40.39%	32.43%	39.91%	16.84
Prior myocardial infarction	10.66%	7.86%	10.49%	9.71
Prior percutaneous coronary intervention	9.38%	6.87%	9.23%	9.22
Prior coronary artery bypass grafting	7.50%	7.13%	7.47%	1.57
Prior pacemaker	2.98%	2.39%	2.94%	3.74
Atrial fibrillation	31.16%	36.10%	31.45%	10.58
Chronic obstructive pulmonary disease	24.86%	21.98%	24.69%	6.78
Prior cerebrovascular disease	7.49%	5.04%	7.34%	9.99
Hypertension	56.44%	48.45%	56.15%	9.67
Peripheral vascular diseases	12.83%	15.55%	12.99%	7.82
Diabetes mellitus	33.16%	38.29%	33.47%	10.90
Obesity	13.45%	18%	13.74%	13.33
Deficiency anemia	20.69%	29.59%	21.23%	20.64
Congestive heart failure	59.20%	67.40%	59.69%	17.28
Chronic renal failure	23.69%	38.56%	24.59%	32.63
Liver disease	3.97%	7.62%	4.19%	15.57
Smokers	31.00%	21.79%	30.44%	20.96
Alcohol abuse	5.51%	5.20%	5.49%	1.24
Weekend admission	24.15%	22.98%	24.08%	2.78
Elixhauser score				54.74
- 0–1	15.02%	4.27%	14.37%	
- 2–3	36.63%	24.23%	35.88%	
- ≥4	48.35%	71.51%	49.75%	
Hospital bed size				14.66
- Small	8.62%	6.21%	8.47%	
- Medium	22.14%	19.52%	21.98%	
- Large	69.24%	74.26%	69.55%	
Expected primary payer				9.48
- Medicare	57.97%	56.03%	57.85%	
- Medicaid	10.30%	12.98%	10.46%	
- Private	22.59%	22.30%	22.58%	
- Other	9.14%	8.69%	9.11%	
Median household income in quartile				5.66
- 1st	29.94%	29.53%	29.91%	
- 2nd	26.22%	24.41%	26.11%	
- 3rd	23.85%	25.73%	23.97%	
- 4th	19.99%	20.33%	20.01%	
Hospital teaching status				21.16
-Rural	5.19%	2.30%	5.02%	
-Urban, non-teaching	28.64%	23.79%	28.35%	
-Urban, teaching	66.17%	73.91%	66.64%	
Type of mechanical circulatory support				
-IABP	21.07%	18.62%	20.92%	6.31
-PVAD	2.07%	3.37%	2.15%	7.92
-ECMO	1.41%	4.87%	1.62%	19.85

¥ASD indicates absolute standardized difference; calculated as differences in means or proportions divided by a pooled estimate of the SD. All p values are significant at 0.05.

Obesity and hypertension were defined by ICD 9 codes ([supplemental table](#)) and dyslipidemia was defined by CCS code ([supplemental table](#)).

Table 2
Baseline characteristics of participants with cardiogenic shock by acute kidney injury requiring dialysis—matched 1:1

Variables	Acute kidney injury requiring dialysis		¥ASD %
	No	Yes	
No. of observation, unweighted	4,457	4,457	
No. of observation, weighted	21,959	21,926	
Age—year, mean (SD)	65.05 (15.62)	63.87 (14.58)	7.77
Women	35.78%	34.97%	1.88
			4.93
- White	65.22%	65.26%	
- Black	16.10%	16.69%	
- Hispanic	9.52%	9.21%	
- Asia	4.27%	3.99%	
Dyslipidemia	32.02%	32.74%	1.25
Prior myocardial infarction	7.63%	8.04%	1.51
Prior percutaneous coronary intervention	7.13%	7.00%	0.79
Prior coronary artery bypass grafting	8.13%	7.37%	2.94
Prior pacemaker	2.52%	2.47%	0.58
Atrial fibrillation	36.50%	36.21%	0.51
Chronic obstructive pulmonary disease	23.13%	22.22%	2.36
Prior cerebrovascular disease	5.42%	5.30%	0.50
Hypertension	52.52%	51.80%	1.35
Peripheral vascular diseases	15.89%	15.65%	0.68
Diabetes mellitus	38.88%	39.12%	0.60
Obesity	17.23%	18.44%	2.99
Deficiency anemia	29.47%	29.68%	0.54
Congestive heart failure	67.86%	67.84%	0.00
Chronic renal failure	38.67%	39.07%	1.01
Liver disease	7.64%	7.89%	0.92
Smoking	22.00%	21.79%	0.43
Alcohol abuse	7.15%	5.20%	7.85
Weekend admission,	22.78%	22.67%	0.27
Elixhauser score			0.00
- 0–1	3.51%	4.00%	
- 2–3	24.06%	23.89%	
- ≥4	72.43%	72.11%	
Hospital bed size, %			0.00
- Small	6.25%	6.13%	
- Medium	19.92%	20.29%	
- Large	73.82%	73.57%	
Expected primary payer, %			2.53
- Medicare	57.17%	56.39%	
- Medicaid	13.12%	13.09%	
- Private	21.39%	21.97%	
- Other	8.32%	8.55%	
Median household income in quartile, %			2.97
- 1st	29.77%	29.93%	
- 2nd	24.14%	23.88%	
- 3rd	25.21%	25.54%	
- 4th	20.88%	20.65%	
Hospital teaching status			2.33
-Rural	2.05%	2.16%	
-Urban, non-teaching	23.90%	24.50%	
-Urban, teaching	74.05%	73.34%	

¥ASD indicates absolute standardized difference; calculated as differences in means or proportions divided by a pooled estimate of the SD. All *p* values are significant at 0.05.

Obesity and hypertension were defined by ICD 9 codes (supplemental table) and dyslipidemia was defined by CCS code (supplemental table).

rates and AKI-HD trends with or without adjustment for demographic, comorbidities, and hospital characteristics (Table 4).

Additionally, we performed subgroup analysis of patients with CS that developed AKI (Supplemental Table 1a). We identified 39,993 patients with CS and AKI who did not utilize HD and 4,930 with AKI-HD (10.96% of the sample). In-patient mortality, use of ECMO, bleeding requiring transfusion, nonroutine discharge, and length of stay were significantly increased among those patients with CS and AKI-HD (Supplemental Table). Patients with AKI-HD were more likely non-Whites, had higher rates of peripheral vascular disease, obesity, chronic renal failure, chronic liver disease, and overall higher prevalence of comorbidities as suggested by distribution of Elixhauser scores (Supplemental Table). In addition, CS patients with AKI-HD were more frequently admitted to larger size and teaching hospitals.

Discussion

In this cohort of 402,825 weighted hospitalizations from the NIS database with cardiogenic shock, we demonstrated that: (1) AKI occurred in approximately half of CS patients, (2) about 11% of CS patients with AKI received HD, (3) the prevalence of comorbidities was higher among patients who utilized HD (4) in-hospital mortality was higher in patients with cardiogenic shock who developed AKI-HD on admission, and (5) health care utilization was increased among patients with AKI-HD as suggested by prolonged hospital stay, increased hospital cost and higher rate of nonroutine home discharge.

Although several studies have identified AKI in CS as a poor prognostic factor, there is lack of data on the in-hospital outcomes of HD utilization to CS patients with AKI. AKI in CS is mainly due to low cardiac output and hypotension-induced renal hypoperfusion and less frequently from contrast-induced nephropathy when PCI is performed in a background of several comorbidities (i.e. advanced age, diabetes, and chronic kidney disease).¹⁰ In our study, AKI occurred in 49% of patients with CS and 6% of the overall CS patients received HD in the setting of AKI. Consistent with these findings, a multicenter study conducted across 54 countries among patients in cardiac and/or coronary care units showed that 5% to 6% had AKI-HD with concomitant increased in hospital mortality.¹¹ In a previous single center study, 55% of patients with CS developed AKI, whereas 1/4 of them received HD.¹⁰ Need of HD was also a predictor of poor outcomes. In the randomized controlled SHOCK Trial of patients with CS after myocardial infarction, AKI occurred in 13% of the patients assigned to emergency revascularization arm, whereas those in the initial medical stabilization arm had a higher prevalence of AKI at 24%.¹² The definition of AKI in this trial was serum creatinine level above 3.0 mg per deciliter which might have underestimated the proportion of patients with AKI. Regardless of the incidence of AKI, the presence of it is a predictor of worse outcomes among patients with CS in the setting of acute myocardial infarction, as suggested by a posthoc analysis of the Global Utilization of Streptokinase and Tissue-Plasminogen Activator for the Occluded Coronary Arteries (GUSTO-I) trial.¹³

Table 3
Clinical outcomes in patients with or without acute kidney injury requiring dialysis

Outcomes	Acute kidney injury requiring dialysis		Odd ratio/mean ratio (95% CI)	p value
	Yes	No		
In-patient mortality	75.74%	51.58%	2.94 (2.67, 3.22)	<.0001
Use of mechanical circulatory support	23.99%	19.27%	1.32 (1.19, 1.46)	<.0001
-ECMO	4.65%	2.39%	1.99 (1.57, 2.53)	<.0001
-PVAD	3.24%	1.76%	1.86 (1.40, 2.46)	<.0001
-IABP	18.57%	16.71%	1.14 (1.02, 1.2)	0.020
Bleeding requiring transfusion	11.38%	7.40%	1.61 (1.39, 1.87)	<.0001
Nonroutine discharge	87.11%	72.70%	2.55 (2.29, 2.84)	<.0001
Cost—mean, \$	80,406	52,833	1.52 (1.44, 1.60)	<.0001
Length of stay* —mean, days	21.35	14.38	1.51 (1.41, 1.61)	<.0001

Length of stay* among those that survived till hospital discharge only.

Table 4
Trend in the incidence of AKI requiring dialysis in patients with cardiogenic shock and mortality trend

	2010	2011	2012	2013	2014	% change/year (p trend)
AKI with HD, Unadj. rate	5.83%	6.06%	6.21%	6.12%	6.44%	+2% p trend: 0.343
AKI with HD, *Adj. rate	2.59%	2.44%	2.46%	2.42%	2.51%	−0.5% p trend: 0.811
Mortality in AKI with HD, Unadj. rate	74.35%	77.52%	76.07%	73.29%	75.60%	−0.3% p trend: 0.721
Mortality in AKI with HD, *Adj. rate	63.62%	67.08%	66.38%	63.62%	65.76%	+0.02% p trend: 0.975

Adjusted for demographic, comorbidities, and hospital characteristics.

*Adj. = adjusted.

Unadj. = unadjusted.

Given the worse mortality among CS patients complicated with AKI, the use of HD has been proposed to improve hemodynamic status by correction of intravascular volume, uremia, and electrolyte derangements. Conversely, we observed an association between AKI-HD and increased mortality. Patients with AKI-HD showed a 2-fold high in mortality than those without HD. This finding is consistent with other previous reports among patients utilizing renal replacement therapy for AKI in settings such as cardiac surgery, septic shock, and contrast-induced nephropathy.^{11,14} Higher prevalence of comorbidities predisposes to development of multiorgan failure and worse outcomes in the setting of CS despite use of renal replacement therapy.^{15,16} In our analysis, after adjusting for patient- and hospital-level comorbidities, in-hospital mortality still increased among patients with CS and AKI-HD. Although it is possible that unmeasured factors have contributed to this, could HD itself raise the risk of complications in this patient population? Patients with indwelling dialysis catheters have an added risk of vascular complications and acquired infections, greatly increasing the odds of sepsis, which in addition to their compromised hemodynamic status may ultimately progress to catastrophic end-organ failure, and death. Thrombi can also form on catheters, leading to serious complications including pulmonary embolism, septic emboli, long-term central venous stenosis, and cardiac arrhythmias, and potential need for systemic anticoagulation. Certainly, adverse effects of HD deserve consideration. However, it is usually the deterioration of hemodynamic condition that leads to HD and subsequently to adverse in-hospital outcomes. The need for HD is an adverse prognostic indicator rather than a cause of adverse outcomes. Hence, early

identification and treatment of CS before development of AKI will likely provide significant clinical benefit.

Our study limitations are primarily related to the accuracy of the ICD-9-CM coding. The NIS database is an administrative database, hence incorrect coding may result in misclassification of cases. Furthermore, information on creatinine clearance as a measure of AKI, type of renal replacement therapy, and timing of the HD are unavailable. However, the NIS data contains rich patient level information which allowed us to use PS matching method to account for various confounding factors.

In summary, our data suggests that patients with cardiogenic shock receiving HD have increased mortality rates. Early identification of CS, treatment of reversible causes, and early initiation of T-MCS when indicated to improve end-organ perfusion are of paramount importance.

Disclosures

No conflicts of interest declared.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.amjcard.2019.02.038>.

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