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Trends in the Incidence of In-Hospital Mortality, Cardiogenic Shock, and Utilization of Mechanical Circulatory Support Devices in Myocarditis (Analysis of National Inpatient Sample Data, 2005−2014)

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ABSTRACT

Background: Myocarditis may be associated with hemodynamic instability and portends a poor prognosis when associated with cardiogenic shock (CS). There are limited data available on the incidence of in-hospital mortality, CS, and utilization of mechanical circulatory support (MCS) devices in these patients.
Methods: We queried the 2005−2014 National Inpatient Sample databases to identify all patients aged >18 years with myocarditis in the United States.
Results: The number of reported cases of myocarditis per 1 million gradually increased from 95 in 2005 to 144 in 2014 (*P*for trend <.01). The trend and incidence of endomyocardial biopsy remained the same despite the increase in clinical diagnosis. Overall, in-hospital mortality was 4.43% of total admissions without a change in overall trend over the study period. We also observed a significant increase in the incidence of CS from 6.94% in 2005 to 11.99% in 2014 (*P*for trend <.01). There was a parallel increase in the utilization of advanced MCS devices during the same time period such as extracorporeal membrane oxygenation or percutaneous cardiopulmonary support (0.32% in 2005 to 2.1% in 2014; *P*< .01) and percutaneous ventricular assist devices such as Impella/tandem heart (0.176% in 2005 to 1.75% in 2014; *P*< .01).
Conclusion: Although the incidence of myocarditis has increased in the last decade, the in-hospital mortality has remained the same despite increases in the incidence of CS, possibly reflecting the benefits of increased usage of advanced MCS devices. We noted that increasing age, presence of multiple comorbidities and CS were associated with an increase in in-patient mortality. (*J Cardiac Fail 2019;25:457−467*)
Key Words: Myocarditis, cardiogenic shock, mechanical circulatory support devices.

Myocarditis is an inflammatory disease of the myocardium diagnosed by clinical and non-invasive imaging findings and confirmed by histopathologic criteria. Endomyocardial biopsy (EMB) is indicated for diagnosis in patients with unexplained new onset fulminant congestive heart failure (CHF) with hemodynamic compromise or in cases of unexplained worsening CHF associated with dilated left ventricle or arrhythmias not responding to conventional medical therapy.[1] Current treatment guidelines recommend general measures to treat underlying etiology and complications including cardiac arrhythmias and CHF.[2] The disease course is highly variable and depends on

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the type of myocarditis and the severity of symptoms. Many patients have subclinical or self-limited disease without long-term complications, others progress to chronic myocarditis and dilated cardiomyopathy, whereas a minority of patients present with fulminant disease requiring hemodynamic support with an intra-aortic balloon pump (IABP), a percutaneous ventricular assist device (pVAD), or extracorporeal membrane oxygenation (ECMO). In some cases of fulminant myocarditis, temporary mechanical circulatory support (MCS) has been used as a bridge to recovery or as a bridge to permanent left-ventricular assist device (LVAD), total artificial heart (TAH), or heart transplantation.[3−12]

To our knowledge, comprehensive, large-scale data on the clinical characteristics, hospitalization, mortality trends, incidence of cardiogenic shock (CS), and utilization of MCS devices in patients with myocarditis are lacking. The aim of our study was to examine the change in the trend of myocarditis, in-hospital mortality, CS, and utilization of different MCS devices using a large U.S. national database.

Methods

Data Sources

This is a retrospective analysis of all hospital admissions for myocarditis between 2005 and 2014. Data were extracted from the NIS, the largest publicly available all-payer inpatient health-care database in the United States including data on ~7−8 million discharges per year and maintained by the Agency for Health Care Quality and Research (AHRQ). A discharge dataset from a 20% stratified sample of U.S. hospitals is recorded in the NIS. Data from the NIS have been used to identify, track, and analyze national trends in health-care usage, patterns of major procedures, access, disparity of care, trends in hospitalizations, charges, quality, and outcomes.[13−16]

Study Population

We collected data on all discharges of adult patients aged ≥18 years with myocarditis using the International Classification of Disease, 9th revision, Clinical Modification (ICD-9-CM) codes, utilized in previous studies[17] (Supplementary Table 1).

Endpoints

Our primary outcomes-of-interest were incidence of CS and utilization of different types of MCS devices, including ECMO/ percutaneous cardiopulmonary support (PCP), pVAD (Impella or tandem heart), IABP, and combined (which included combination of any of these devices together during index hospital admission) and all cause in-hospital mortality. These outcomes were captured from the dataset with ICD-9-CM codes (Supplementary Table 1). Other secondary outcomes included utilization of EMB, right heart catheterization (RHC) in patients with CS, cost of hospitalization, and duration of hospitalization (length of stay in days [LOS]) and the incidence of patients bridged to LVAD or TAH during the same hospitalization.

To calculate the estimated cost of hospitalizations, the NIS data were merged with cost-to-charge ratios available from the Healthcare Cost and Utilization Project. We estimated the cost of each inpatient stay by multiplying the total hospital charge by the cost-to-charge ratio. Confounding factors which could impact hospital outcomes were also selected from the datasets either as already provided variables or abstracted with the ICD-9-CM codes. Furthermore, we used comorbid conditions to derive the Elixhauser Comorbidity Index, a well validated tool for prediction of in-hospital mortality and readmission (Supplementary Table 2).[18,19] The hospital characteristics were also derived from the dataset and recorded as hospital region, hospital teaching status, and hospital bed-size. The hospital bed-size classification was done with the Core Based Statistical Area designations, and this varied with the regions. A hospital was designated as small, medium, and large such that one-third of the hospitals in a given region, teaching status, and location would fall within that category.

Statistical Analysis

As per recommendations of the AHRQ, we used survey analysis methods to account for clustering and stratification of patients for all continuous and categorical variables.[20] All data extractions and analyses were done with the Statistical Analysis System (SAS V.9.4, SAS Institute Inc, Cary, NC). We chose a P value $< .05$ as being statistically significant; we reported the effect sizes, 95% confidence intervals (CI), and P values. We reported the mean and SD for continuous variables and percentages for categorical variables. Baseline characteristics of survivors and non-survivors were compared with independent paired t tests for continuous variables with normal distribution, and chi-square tests for categorical variables.

Myocarditis hospitalization rates were expressed as the diagnosis of myocarditis/million total hospitalizations, calculated by dividing the total estimated number of myocarditis hospitalizations by the total number of admissions in the United States multiplied by 1 million. We used sampling weights to estimate trends and national estimates to account for the change in sampling design as recommended by the AHRQ. Specifically, to account for the differences in sampling strategy from 2012 to 2014, compared with before 2012, revised discharge weights termed "trend weights" were used for 2011 and all preceding years while computing national estimates to ensure comparability across years and to facilitate trend analysis.[21]

The trend in myocarditis hospitalizations per million hospitalizations was evaluated using the Cochrane Armitage test. Discrete numeric variables with an over-dispersed count distribution (LOS) and continuous variables with a right-skewed spread (total hospital cost) were modeled with generalized linear regressions, and with a negative binomial function and gamma function respectively and trends in geometric means were examined. For analysis of the calendar year trends in mortality, we adjusted for trends in patient characteristics over time using a multivariable logistic regression model for survey data (SURVEYLOGISTIC) and accounted for hospital-level clustering of patients and the sampling design in our models using CLUSTER and STRATA statements, respectively. We also used multivariable logistic regression to identify independent predictors of mortality, the occurrence of CS and the use of MCS devices.

Results

Baseline Characteristics

Between 2005 and 2014 there were 36,967 patients admitted for myocarditis. Of these, 1648 (4.46%) patients died, whereas 35,319 patients survived to hospital discharge (95.54%). The baseline characteristics were significantly different between patients with and without in-hospital mortality as shown in Table 1. Compared with survivors, patients who died were on an average older (51.8 vs

Table 1. Baseline Characteristics of Myocarditis Patients With and Without In-Hospital Mortality

	In-Hospital Mortality	Without In-Hospital Mortality	*P*
	N (%)/Mean (SD)	N (%)/Mean (SD)	
No. of observations	1648 (4.46)	35,319 (95.54)	
Age (years)	51.83 ± 18.91	43.65 ± 17.77	<.01
Female	48.45	38.44	<.01
Race			
Whites	63.36	68.32	<.02
Blacks	21.11	14.67	
Hispanics	7.57	9.95	
Others[§]	7.96	7.06	
Chronic medical conditions (%)			
Cardiac arrhythmia	5.33	3.03	.02
Hypertension	29.36	31.37	.44
Hypothyroidism	7.69	6.68	.49
Chronic liver disease	3.87	2.15	.05
Diabetes	14.52	11.42	.08
Obesity	7.35	11.08	.03
Chronic pulmonary vascular disease	5.96	2.37	<.01
Chronic lung disease	15.13	14.01	.56
Congestive heart failure	31.98	14.86	<.01
Deficiency anemia	15.73	12.54	.11
Coagulopathy	28.57	7.1	<.01
Chronic kidney Disease	17.46	6.42	<.01
Peripheral vascular disease	5.05	2.21	<.01
Metastatic cancer	2.04	0.52	<.01
Lymphoma	4.04	0.74	<.01
Electrolyte derangement	60.47	26.03	<.01
Alcohol abuse	4.45	3.79	.56
Elixhauser comorbidities			<.01
0	9.43	27.26	
1−3	52.93	56.39	
>4	37.64	16.35	
Expected primary payer			
Medicare	30.39	17.39	<.01
Medicaid	18.84	13.24	
Private	39.95	54.03	
Others[||]	10.82	13.34	
Median household income in quartile			
1st	24.25	22.6	.43
2nd	26.3	23.89	
3nd	25.09	25.36	
4th	24.37	28.15	
Hospital bed side			
Small	7.78	10.85	.18
Medium	21.3	22.58	
Large	70.93	66.57	
Hospital teaching status			
Rural	4.05	7.59	<.01
Urban, nonteaching	21.94	34.86	
Urban, teaching	74.01	57.55	
Hospital ownership			
Government, nonfederal	16.28	10.59	.01
Private, not for profit	72.44	78.36	
Private for profit	11.27	11.04	

[§]Represents other races excluding White, Blacks and Hispanics.
[||]Self pay, no charge and other modalities of payment.

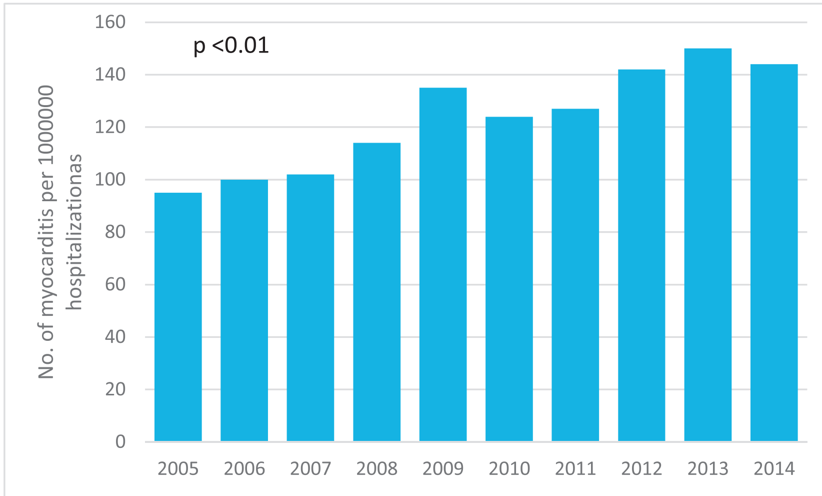

Fig. 1. Trend in myocarditis cases per 1,000,000 from 2005 to 2014.

43.6 years, $P < .01$), more likely to be females (48.5% vs 38.44%, $P < .01$), of African-American descent (21.11% vs 14.67%, $P = .02$) and had a significantly higher likelihood of associated CHF, chronic pulmonary vascular disease, coagulopathy disorder, metastatic cancer, electrolyte derangement, and chronic kidney disease ($P < .05$). Patients with in-hospital mortality were more likely to have more than 4 Elixhauser comorbidities (37.64% vs 16.35%, $P < .01$), whereas patients who survived were more likely to have 0 Elixhauser comorbidities (27.26% vs 9.43%, $P < .01$; refer to Supplementary Table 2 for details on Elixhauser comorbidities).

Main Outcomes

The number of reported cases of myocarditis per 1,000,000 gradually increased from 95 in 2005 to 144 in 2014 (Fig. 1). Table 2 shows annual outcomes of in-patient mortality, CS, performance of RHC, and utilization of MCS devices. The overall frequency of in-hospital mortality was 5.33% in 2005 compared with 6.41% in 2014 ($P = .48$). The annual prevalence of CS showed a significant increase from 6.9% in 2005 to 11.9% in 2014 ($P < .01$). In-hospital mortality of patients with CS between 2005 to 2014 averaged 22.65%, which was significantly higher than those without CS (2.65%). In all, 31.97% of patients with CS underwent RHC; the incidence of overall mortality in those with CS who underwent RHC was 18.94%; in contrast, patients with CS and myocarditis who did not undergo a RHC had higher overall mortality of 24.3%. No significant trend of RHC usage was apparent over this time period.

There was a longitudinal increase in utilization of advanced MCS devices including ECMO (0.32% in 2005 to 2.1% in 2014), pVADs such as Impella/tandem heart (0.18% in 2005 to 1.75% in 2014), and combined MCS devices (0.16% in 2005 to 1.63% in 2014), which were all

Table 2. Trend of Outcomes of In-Hospital Mortality, Cardiogenic Shock, Right Heart Catheterization, and Utilization of Different Types of MCS Devices

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Overall	*P* Value for Trend
In-Hospital mortality %	5.27	5.25	3.19	4.13	4.35	5.30	3.30	3.77	4.22	6.41	4.46	.48
Cardiogenic shock %	6.94	5.63	6.94	7.46	9.42	8.60	9.82	9.83	10.88	11.99	8.95	<.01
In-hospital mortality in patients with cardiogenic shock %	30.17	40.73	24.63	13.72	19.01	28.69	17.70	17.44	20.62	28.16	22.65	.49
In-hospital mortality in patients without cardiogenic shock %	3.35	2.90	1.59	3.36	2.83	3.04	1.48	2.28	2.24	3.44	2.65	.70
Right heart catheterization (RHC)												
RHC % in Cardiogenic shock	22.92	39.97	26.67	34.93	38.03	43.66	28.09	27.91	34.69	26.21	31.97	.647
Mortality in cardiogenic shock with RHC %	10.47	30.25	15.21	14.77	15.58	32.81	15.48	12.50	11.76	29.63	18.94	.778
Mortality in cardiogenic shock without RHC %	36.03	47.71	28.06	13.16	21.12	25.50	18.58	19.35	25.40	27.63	24.27	.361
Mechanical circulatory support devices												
% ECMO/PCP	0.32	0.15	0.15	0.13	0.78	0.87	0.58	0.91	2.00	2.10	0.86	<.01
% PVAD	0.176	0.00	0.15	0.26	0.78	0.75	1.39	0.91	1.33	1.75	0.81	<.01
% IABP	3.87	4.00	3.17	5.01	4.04	4.61	3.46	4.00	3.11	3.14	3.83	.24
Combined %	0.16	0.15	0.15	0.13	0.11	0.62	0.58	0.57	0.89	1.63	0.53	<.01
Vasopressors use %	9.63	5.15	20.93	10.28	8.57	6.75	10.90	13.95	10.85	6.12	9.86	.615

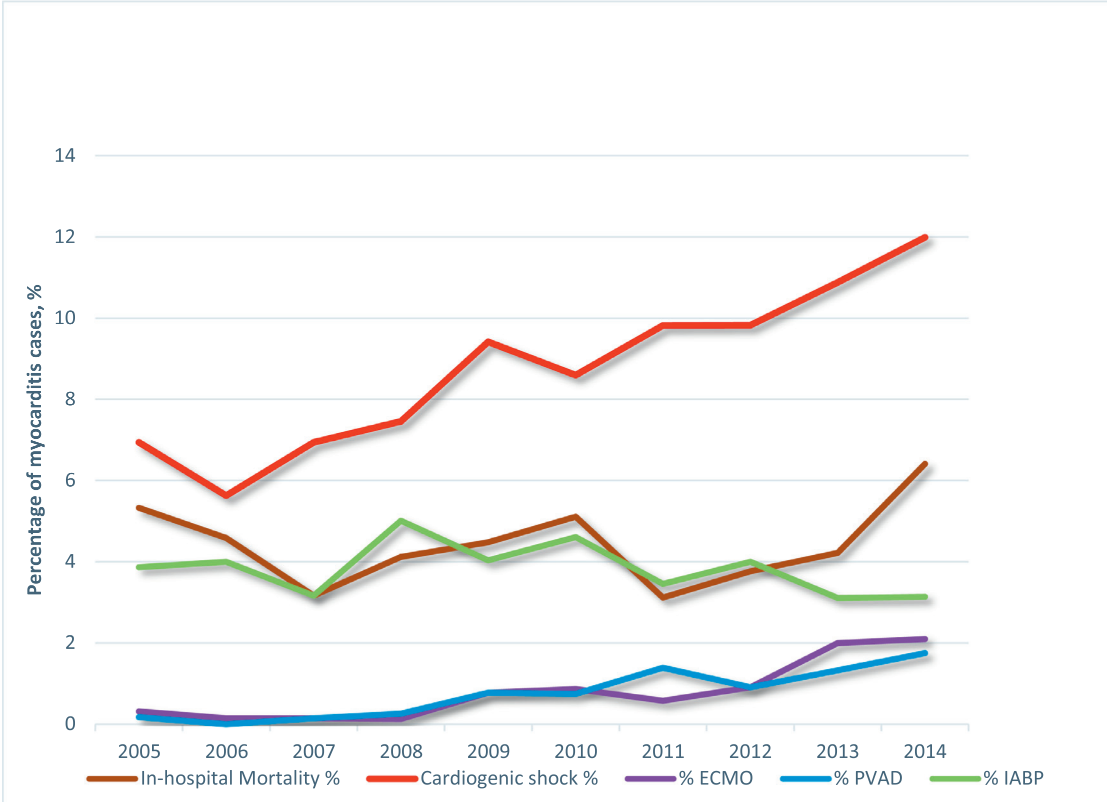

Fig. 2. Trends of In-hospital mortality, cardiogenic shock, and mechanical circulatory support devices (ECMO, IABP, and PVAD).

statistically significant ($P < .01$) as shown in Table 2. However, we also noted decreased utilization of IABP starting ~2012 that appears to coincide with the advent and availability of other forms of MCS devices (Fig. 2). We found that 6.72% of patients with myocarditis were bridged to LVAD and 0.84% to TAH. There was no significant trend in the incidence of bridging to LVAD/TAH over the study period. We also found that 1451 of a total of 36,967 patients with myocarditis were transferred from one center to another, of these, 405/1451 (27.9%) had cardiogenic shock.

The average incidence of EMB was 3.24%, with no change in trend from 2005 to 2014 (Table 3). The total cost of hospitalization was $25,992, but there was no significant change in cost of hospitalization or overall length of hospital stay, which was ~6−7 days (Table 3).

Predictors of In-Patient Mortality, CS, and MCS Utilization

Multivariable regression analysis identified several independent predictors of mortality (Table 4). For every 5-year increase in age, there was a 12% increase in the risk of mortality (aOR: 1.12, 95%CI: 1.05−1.19, $P < .01$), similarly, with every 2-point increase in Elixhauser score, there was a 35.7% increased risk of mortality (aOR: 1.35, 95% CI: 1.14− 1.60, $P < .01$). Patients of African-American descent were 55% more likely to die compared with Caucasians (aOR: 1.557, 95% CI: 1.016−2.386; $P = .04$). Concomitant CS (aOR: 2.48, 95% CI: 1.75−4.7, $P < .01$), vasopressor use (aOR: 2.48, 95% CI: 1.19−5.16, $P = .02$), and cardiac arrest (aOR: 9.0, 95% CI: 5.00−16.32, $P < .01$) were each associated with a significantly higher risk of mortality.

Table 3. Trends of Outcomes of Endomyocardial Biopsy, Hospital Cost, Length of Stay, and Nonroutine Home Discharge

	2005	2006	2007	2008	2009	2010	2011	2012	2013		Overall	*P*
% EMB (endomyocardial biopsy)	2.88	6.80	2.71	3.54	3.95	3.02	2.88	2.97	3.44	3.03	3.24	.44
Average hospital cost ($)	25,314	22,046	27,861	24,483	29,179	25,219	26,457	24,451	27,753	26,518	25,992	.230
Average length of hospital stay (days)	6.75	5.88	5.45	6.76	7.6	6.47	6.41	6.3	6.8	6.94	6.56	.33
% of Nonroutine home discharge	27.26	25.04	24.43	26.99	24.89	25.31	25.56	24	26.53	30.15	26.14	.20

Table 4. Predictors of In-Patient Mortality

Variables	Estimate OR	95% Confidence Limits		P
		LL	UL	
Age every 5 years	1.12	1.052	1.192	<.01
Elixhauser score every 2 units increase	1.357	1.146	1.606	<.01
Female vs male	1.116	0.82	1.519	.48
Race				
Caucasians (ref.)				
African Americans	1.557	1.016	2.386	.04
Hispanic	0.934	0.509	1.713	.83
Others[§]	1.043	0.565	1.924	.89
Median Household income in quartile				
1st (ref.)				
2nd	1.084	0.695	1.691	.72
3nd	1.07	0.679	1.687	.77
4th	0.926	0.568	1.51	.76
Hospital regions				
Northeast (ref.)				
Midwest	0.736	0.429	1.261	.26
South	1.289	0.803	2.072	.29
West	1.073	0.635	1.814	.79
Hospital bed size				
Small (ref.)				
Medium	1.376	0.772	2.452	.28
Large	1.27	0.764	2.111	.36
Location/teaching status of hospital				
Rural (ref.)				
Urban nonteaching	0.921	0.461	1.838	.82
Urban teaching	1.492	0.768	2.899	.24
Expected primary payer				
Medicare (ref.)				
Medicaid	0.926	0.498	1.72	.81
Private	0.631	0.388	1.028	.06
Others[||]	0.745	0.407	1.364	.34
Mechanical Circulatory Support Devices				
ECMO/PCP	5.544	2.16	14.226	<.01
IABP	1.581	0.864	2.893	.14
PVAD	3.117	1.094	8.877	.03
Vasopressor use	2.481	1.193	5.16	.02
Cardiogenic shock	2.874	1.758	4.699	<.01
Ventricular fibrillation	0.875	0.345	2.222	.78
Cardiac arrest	9.038	5.003	16.327	<.01

ref. - Reference group.
[§]Represents other races excluding White, Blacks and Hispanics.
[||]Self pay, no charge and other modalities of payment.

We also evaluated risk factors predicting the occurrence of CS (Table 5). CS was found to be more common in females (aOR: 1.34, 95% CI: 1.07−1.68, $P = .01$) and in lower income strata (ie, the 4th quartile of median household income) were at increased risk of experiencing CS (aOR: 1.42, 95% CI: 1.02−1.97, $P = .03$). Similar to mortality, we noted that with every 2-point increase in the Elixhauser Comorbidity Index, the risk was increased by 1.62 times (aOR: 1.62, 95% CI: 1.44−1.81, $P < .01$). The presence of concomitant ventricular fibrillation (aOR: 3.32, 95% CI: 1.79−6.16, $P < .01$), cardiac arrest (aOR: 7.24, 95% CI: 4.73−11.09, $P < .01$), and vasopressor use (aOR: 6.51, 95% CI: 3.82−11.10, $P < .01$) were also found to be associated with the presence of CS. Patients admitted to the large hospitals were at higher risk compared with small bed size hospitals (a0R: 2.14, 95% CI: 1.36−3.36, $P < .01$) to have CS.

In addition, predictors of MCS device placement are summarized in Table 6. Hispanic patients were 31.4% less likely to receive MCS therapy than Caucasians (aOR: 0.314, 95% CI: 0.154−0.64, $P < .01$). As expected, devices were more commonly placed in large hospitals compared with smaller hospitals (aOR: 2.39, 95% CI: 1.19−4.80, $P = .01$). The likelihood of receiving MCS was not independently influenced by age, gender, Elixhauser Comorbidity Index, median household income, location/teaching status of the hospital, or expected primary payer.

Discussion

Utilizing the largest U.S. national hospitalizations database, this report describes clinical outcome data on in-hospital mortality, the incidence of CS and trends in MCS device use in patients with myocarditis in the United States over a decade. The main findings of our analysis are as follows: 1) The overall incidence of myocarditis has gradually trended up with an aggregate in-hospital mortality remaining stable and estimated at ∼4.43%. 2) The utilization of EMB has remained the same despite an increase in clinical

Table 5. Predictors of Cardiogenic Shock

Variables	Estimate	95% Confidence Limits		*P*
	OR	LL	UL	
Age every 5 years	1.023	0.988	1.059	.20
Elixhauser score every 2 units increase	1.62	1.445	1.817	<.01
Female vs Male	1.346	1.076	1.684	.01
Race				
Caucasians (ref.)				
African Americans	0.994	0.733	1.348	.97
Hispanic	0.663	0.439	1	.05
Others[§]	1.565	1.075	2.278	.02
Median Household income in quartile				
1st (ref.)				
2nd	1.137	0.829	1.558	.42
3nd	1.131	0.825	1.551	.44
4th	1.423	1.026	1.974	.03
Hospital regions				
Northeast (ref.)				
Midwest	1.291	0.932	1.789	.12
South	1.223	0.91	1.643	.18
West	1.884	1.367	2.597	<.01
Hospital bed size				
Small (ref.)				
Medium	1.23	0.751	2.017	.41
Large	2.144	1.367	3.363	<.01
Location/teaching status of hospital				
Rural (ref.)				
Urban nonteaching	1.386	0.724	2.65	.32
Urban teaching	3.589	1.936	6.65	<.01
Expected primary payer				
Medicare (ref.)				
Medicaid	1.604	1.083	2.377	.02
Private	1.142	0.831	1.57	.41
Others[||]	0.92	0.604	1.402	.70
Ventricular fibrillation	3.326	1.796	6.161	<.01
Cardiac arrest	7.246	4.735	11.09	<.01
Vasopressor use	6.516	3.825	11.101	<.01

ref. - Reference group.
[§]Represents other races excluding White, Blacks and Hispanics.
[||]Self pay, no charge and other modalities of payment.

diagnosis of myocarditis. 3) The incidence of CS almost doubled during the study period 2005−2014. 4) A rising trend in the utilization of advanced MCS devices, such as ECMO/PCP, Impella/tandem heart, was also observed, whereas IABP usage has declined.

The increase in clinical diagnosis of myocarditis despite no change in the trend of EMB is most likely because of the increase utilization of advanced imaging and clinical awareness. However, because of the lack of specific ICD-9 codes for cardiac MRI in the NIS database, we are unable to corroborate this speculation with supportive data. The contemporary diagnosis of myocarditis is based on both the clinical presentation and the application of advanced CMR imaging techniques, given its unique ability to identify myocardial edema, inflammation, fibrosis, and necrosis.[22,23] EMB is indicated in the setting of fulminant CHF with hemodynamic compromise or in cases of unexplained CHF associated with dilated left ventricle and ventricular arrhythmias, conduction heart block (Mobitz type II or complete heart block).[1]

There are currently insufficient data describing the incidence and predictors of mortality in patients with myocarditis.[24] We observed that the patients with in-hospital mortality were older compared with those who survived. This was observed in a similar study by Xu et al,[25] which examined predictors of in-hospital mortality in patients with myocarditis and found that age ≥50 was a significant predictor of mortality (OR: 7.43 [2.18−25.34], $P < .001$). We also noted in addition to increasing age, patients with multiple comorbidities (indexed by higher Elixhauser scores) and African-American descent were at higher risk of mortality.

The incidence of mortality in patients with CS was much higher compared with those without CS. Patients with hemodynamically stable myocarditis can rapidly decline and develop CS due to severe ventricular dysfunction as a result of pump failure from severe inflammation of the myocardium. As expected, we noted that the presence of CS and vasopressin use were associated with an increased risk of mortality which was consistent with previous studies.[3,26]

Most hemodynamically stable patients will respond to conservative medical management, which includes supportive care, whereas those with circulatory collapse require immediate MCS device support to provide time for diagnosis and to initiate medical therapy.[27−31] These patients should be referred immediately to an intensive care unit

Table 6. Predictors of Mechanical Circulatory Support Device Use

Variables	Estimate	95% Confidence Limits		*P*
	OR	UL	LL	
Age every 5 years increase	1.028	0.966	1.093	.39
Elixhauser score every 2 units increase	0.879	0.733	1.056	.17
Female vs Male	0.905	0.669	1.225	.52
Race				
Caucasians (ref.)				
African Americans	1.15	0.75	1.763	.52
Hispanic	0.314	0.154	0.64	<.01
‡Others	1.153	0.654	2.033	.62
Median Household income in quartile				
1st (ref.)				
2nd	1.018	0.625	1.657	.94
3nd	1.373	0.844	2.235	.20
4th	1.217	0.759	1.951	.41
Hospital regions				
Northeast (ref.)				
Midwest	0.789	0.456	1.367	.40
South	1.448	0.954	2.2	.08
West	0.951	0.579	1.562	.84
Hospital bed size				
Small (ref.)				
Medium	2.005	0.956	4.205	.07
Large	2.399	1.198	4.804	.01
Location/teaching status of hospital				
Rural (ref.)				
Urban nonteaching	1.702	0.671	4.316	.26
Urban teaching	1.91	0.775	4.711	.16
Expected primary payer				
Medicare (ref.)				
Medicaid	1.257	0.678	2.33	.47
Private	1.228	0.73	2.065	.44
Others[||]	1.022	0.541	1.93	.95
Cardiogenic Shock	55.112	36.936	82.233	<.01
Ventricular fibrillation	1.275	0.598	2.715	.53
Cardiac arrest	2.629	1.499	4.609	<.01
Vasopressor use	0.967	0.474	1.972	.93

ref. - Reference group.

with respiratory and mechanical cardiopulmonary support facilities.[26] This was noted in our findings with higher association of CS and MCS use in larger-sized hospitals compared with smaller hospitals. Early utilization of MCS devices may help reduce wall stress, cytokine activation, improve myocardial contractility, and favorably influence ventricular geometry.[32] The use of MCS devices in myocarditis is a relatively unexplored area and several questions remain unanswered. There are limited observational studies describing use of different types of MCS devices and their benefits.[27−33]

To our knowledge, our study is the largest study examining the use of different types of MCS devices in patients with myocarditis. We noticed increase in use of MCS devices from 4.3% in 2005 to 6.9% in 2014, which mirrors the rising incidence of CS reported in our study. Previous studies have shown increasing utilization of ECMO as the preferred MCS device for CS.[34] We noticed a similar trend with increased use of ECMO and percutaneous ventricular assist devices such as Impella/tandem heart. A recent analysis of the CVAD registry identified a 62% survival to discharge rate among myocarditis patients receiving Impella support.[35]

Although all MCS devices improve cardiac output and blood pressure in patients with myocarditis they have different overall hemodynamic effects, particularly as they relate to impact on left ventricular (LV) unloading and pulmonary capillary wedge pressure (PCWP). There are limited data examining the implications of these differences on clinical outcomes. The choice of MCS device depends on whether CS is related to left ventricular dysfunction or biventricular failure. For instance, IABP provides minimal support, whereas Impella/tandem heart can provide LV unloading, enhance forward cardiac output, and improved systemic perfusion. LV unloading by Impella has been independently associated with reduced myocardial inflammation in myocarditis.[36] On the other hand, in patients with biventricular failure, ECMO has traditionally been cited as the preferred device.[30,34,37] However, although ECMO can provide right ventricular unloading, it can significantly increase LV afterload pressure, LV end-diastolic pressure, LV wall stress, and PCWP; each of these factors can potentially leading to LV dilation and dysfunction resulting in cardiac remodeling. Utilization of ECMO in patients with isolated LV dysfunction has been associated with worse outcomes than in patients with biventricular or isolated left ventricular failure.[38] We noted that the presence of ECMO alone was associated with higher risk of mortality (OR: 5.54, CI: 2.16−14.23, $P < .01$), which was highest among all the MCS devices. In contrast, the simultaneous use of ECMO plus a pVAD, such as Impella, can help mitigate the adverse effects on LV wall stress, myocardial oxygen demand, LV end diastolic pressure, PCWP, and the inflammatory response associated with a stand-alone ECMO device.[36]

Most patients with CS in myocarditis recover completely after short-term MCS device use. However, a small number of patients that are refractory may require LVAD or biventricular support as a bridge to TAH.[39,40] These patients need to be evaluated for heart transplant. This is especially the case for patients with giant cell myocarditis who rarely recover, can progress quickly, and may benefit from early listing for heart transplant.[41] In our study, from among all patients with CS ∼69.7% recovered either with MCS or medical therapy, 22.65% died, and 7.56% of patients were bridged to LVAD (6.72%) or TAH (0.84%).

Limitations

Several limitations of this study need to be acknowledged. First, NIS is a de-identified administrative database making it impossible to validate individual ICD-9 codes, this deficiency could potentially have impacted our myocarditis trend analysis, nevertheless, the same codes were followed through the entire study period. Further, our results comport with prior studies from the same database reporting increasing trends of overall CS[42] and increased utilization of short-term MCS with decreasing in-hospital mortality.[43] In aggregate, these data only represent associations and do not in any way imply causality. It is important to note that in-hospital mortality in patients with shock has not significantly declined despite the increase in use of devices.

Because administrative databases lack patient-specific clinical details related to demographics and therapies typically available in trials and registries, extracted analyses are susceptible to errors of coding. Similarly, because the study is based on principal hospital admission, it lacks data on long-term follow-up. These limitations are counterbalanced by a larger sample size and absence of reporting bias, which usually results from selective publications from specialized centers. We were also unable to determine whether patients were switched from one MCS device to another in the same hospital admission because the codes only identified the MCS device used during the principal hospital admission.

Conclusion

In conclusion, we noted an increase in the diagnosis of myocarditis from 2005 to 2014. The in-hospital mortality has remained the same, despite a significant increase in the incidence of CS. We also noted that increasing age and the presence of CS were associated with an increased risk of mortality. Furthermore, the presence of multiple comorbidities was associated with a higher risk of CS and mortality in myocarditis. Future randomized controlled studies are needed to finesse device usage and better define the role of MCS in reducing mortality in these patients.

Disclosures

No conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2019.04.012.

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