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Palliative Care Services in Patients Admitted With Cardiogenic Shock in the United States: Frequency and Predictors of 30-Day Readmission

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ABSTRACT

Background: Patients admitted with cardiogenic shock (CS) have high mortality rates, readmission rates, and healthcare costs. Palliative care services (PCS) may be underused, and the association with 30-day readmission and other predictive factors is unknown. We studied the frequency, etiologies, and predictors of 30-day readmission in CS admissions with and without PCS in the United States.

Methods and Results: Using the 2017 Nationwide Readmissions Database, we identified admissions for (1) CS, (2) CS with PCS, and (3) CS without PCS. We compared differences in outcomes and predictors of readmission using multivariable logistic regression analysis accounting for survey design. Of 133,738 CS admissions nationally in 2017, 36.3% died inpatient. Among those who survived, 8.6% used PCS and 21% were readmitted within 30 days. Difference between CS with and without PCS groups included mortality (72.8% vs 27%), readmission rate (11.6% vs 21.9%), most frequent discharge destination (50.2% skilled nursing facilities vs 36.4% home), hospitalization cost per patient (\$51,083 ± \$2,629 vs \$66,815 ± \$1,729). The primary readmission diagnoses for both groups were heart failure (32.1% vs 24.4%). PCS use was associated with lower rates of readmission (odds ratio, 0.462; 95% confidence interval, 0.408–0.524; $P < .001$). Do-not-resuscitate status, private pay, self-pay, and cardiac arrest were negative predictors, and multiple comorbidities was a positive predictor of readmission.

Conclusions: The use of PCS in CS admissions remains low at 8.6% in 2017. PCS use was associated with lower 30-day readmission rates and hospitalization costs. PCS are associated with a decrease in future acute care service use for critically ill cardiac patients but underused for high-risk cardiac patients. (*J Cardiac Fail* 2021;27:560–567)

Key Words: Cardiogenic shock, palliative care services, health services and outcomes, readmission.

Cardiogenic shock (CS) often occurs as a complication of acute myocardial infarction (AMI) and/or end-stage heart failure and cause a significant burden to patients and to society. Patients admitted with CS have high inpatient mortality of approximately 27% to approximately 51% and high

hospitalization costs owing to the use of advanced circulatory support therapies.^{1–3} The hospitalization costs for CS complicating AMI had been cited between \$41,000 to \$126,000 and readmission rates had been cited at 18%–22%.^{4–7} Unfortunately, there are often significant discrepancies between patients' perceived prognosis of their cardiovascular disease state compared with the actual predicted prognosis.⁸ This gap in knowledge may affect patients' ability to make appropriate end-of-life decisions that are consistent with their goals of care. Therefore, among high-risk patients for adverse events and poor outcomes, palliative care services (PCS) are appropriate for assisting with shared decision making and directing goals of treatment during and after critical illness.⁹ PCS can provide social, emotional, and spiritual support to patients and families and has been used in hospitalizations for myriad of illnesses such as acute decompensated heart failure and cancer.^{4,9,10} Palliative care is distinct from hospice and comfort care, and can decrease physical symptoms, improve quality of life, and complement curative therapies.^{3,9–11} A recent randomized, controlled study in patients with

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advanced heart failure found that PCS in addition to usual care had a clinically significant improvement on the Kansas City Cardiomyopathy Questionnaire, overall functional assessment as well as depression and anxiety compared with usual care alone.¹² Despite the American Heart Association's recommendation of PCS in CS regardless of candidacy for mechanical circulatory support, a recent retrospective National Inpatient Sample study from 2000 to 2014 found only 4.5% of hospitalizations for CS complicating AMI used PCS.⁴ In another national cohort study using the Veterans Affairs External Peer Review Program data from 2007 to 2013, only 7.6% of 4474 patients received PCS up to 1 year after heart failure hospitalization.¹³ Although consultation with the palliative care team is mandated for patients undergoing left ventricular assist device or cardiac transplant evaluation by Medicare and Medicaid Services,^{14,15} its use in other patients admitted with CS and its impacts on readmission outcomes are not well-known. We hypothesize that PCS are underused in patients admitted with CS, but has a significant overall impact on readmission outcomes. We studied the frequency, etiologies, and predictors of 30-day readmission in hospitalized patients admitted with CS who received PCS in the United States in 2017.

Methods

Data

We used the 2017 Healthcare Cost and Utilization Project's (HCUP) Nationwide Readmissions Database (NRD).¹⁶ The study was determined as exempt by the University of California, Los Angeles, Institutional Review Board. The NRD is developed for the HCUP and addresses and includes information for hospital readmission for patient of all ages. The 2017 NRD represents almost one-half of all US hospitalizations from 2454 hospitals from 28 states, which contains data from approximately 18 million unweighted discharges; after weighting, it represent the 36 million national hospitalizations. The 2017 NRD database uses the *International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System* (ICD-10-CM/PCS) diagnosis and procedures (relevant codes used in Supplementary Table 1). Patient demographics (including sex, age, median household income quartile, and urban/rural location), payment sources, total charges, and hospital costs are included in the NRD (Table 1). We used the ICD-10-CM code Z51.5 (equivalent to ICD-9-CM code V66.7) to identify patients receiving PCS. Its use for inpatient hospitalization has been validated with more than 98% specificity in various studies and has been used in previous studies using the HCUP National Inpatient Sample database.^{4,17–19}

Study Population

We identified index admissions in patients with (1) CS (ICD-10-CM code R57.0, T81.11XA, T81.11XD, T81.11XS) (Supplementary Table 1), (2) CS with PCS

(ICD-10-CM code Z51.5), and (3) CS without PCS between January 1, 2017, and November 30, 2017. Patients with orthotopic heart transplantation or left ventricular assist device were excluded given the Center for Medicare and Medicaid services' mandate for PCS in those patients.^{14,15} The index admission variables were created using the first admission for CS with and without PCS of the year. Hospitalizations were excluded if the patient was under 18 years of age, died during the index admission, had an unknown length of stay, or was discharged in the month of December. Readmission variables was created by using the hospital visit numbers and only the first readmission within 30 days of the index admission.

Primary Measures

We assessed the baseline patient characteristics by PCS status including age, sex, do-not-resuscitate (DNR) status, index admission mortality rate, length of stay, total hospitalization cost, primary insurance payer, median household income by quartile, discharge location, and cardiovascular comorbidities by ICD-10-CM. We investigated hospital characteristics including bed size, teaching status, and ownership of the hospital.

We identified the time to readmission by using the difference in days between discharge from the index admission and the first readmission. The readmission outcomes included the frequency and primary etiologies of 30-day readmission in patients with and without PCS during index admission. Independent predictors of 30-day readmission were also analyzed, including PCS, DNR status, age, sex, length of hospitalization, health insurance, income, disposition, hospital characteristics (including bed size, teaching status, and ownership), comorbidities, and procedures (Supplementary Table 1). We performed a subgroup analysis to assess for differences in predictors between the PCS and the non-PCS groups Table 2.

Statistical Analysis

Weighted estimates were calculated by the Agency for Healthcare Research and Quality recommended method using survey and cluster adjustments per NRD design.²⁰ Predictors of 30-day readmission were evaluated using survey weighted logistic regression analysis with cluster adjustments in Stata 16.1 software (StataCorp, Inc., College Station, TX). Multivariable fractional polynomial model selection was used to assess model fit for continuous covariates. Predictors of 30-day readmission are presented as odds ratios (OR) with 95% upper and lower confidence intervals (CI).

Results

Index Admission Variables and Frequency of Readmission

An estimated 14,427 (survey-weighted) patients were excluded for being under 18 years of age, lacking length of

Table 1. Baseline Characteristics of the Cohort Cardiogenic Shock Population on Index Admission, Stratified by PCS Use (Survey Weighted, Excluding Patients Who Died During the Index Admission)

Characteristics	PCS Group			Non-PCS Group		
	Overall (N = 7326)	Readmitted (n = 850)	Not readmitted (n = 6476)	Overall (N = 77,882)	Readmitted (n = 17,036)	Not readmitted (n = 60,846)
Total patients	100%	11.6%	88.4%	100%	21.9%	78.1%
Age, average (y)	70.7	64.9	71.4	63.8	64.5	63.6
18–49	7.6%	12.6%	6.9%	13.0%	13.1%	13.0%
50–64	22.5%	33.1%	21.1%	32.2%	31.8%	32.4%
65–79	38.3%	39.3%	38.2%	40.2%	40.2%	40.2%
≥80	31.6%	15.0%	33.8%	14.5%	14.8%	14.5%
DNR status	61.3%			7.3%		
Female	39.1%	33.2%	39.9%	35.9%	37.2%	35.5%
Insurance						
Medicare	72.7%	65.6%	73.7%	60.2%	64.2%	59.1%
Medicaid	10.0%	20.1%	8.6%	12.0%	13.8%	11.5%
Private	11.4%	11.0%	11.4%	21.6%	17.0%	22.9%
Self-pay	1.5%	1.4%	1.6%	2.7%	2.0%	2.9%
Other	4.1%	1.8%	4.4%	3.0%	2.5%	3.1%
Household income (percentiles)						
0–25th	31.6%	35.3%	31.1%	29.9%	31.7%	29.4%
26th–50th	27.6%	31.0%	27.1%	28.0%	27.7%	28.1%
51st–75th	23.2%	18.2%	23.9%	23.2%	22.9%	23.3%
76th–100th	16.2%	13.0%	16.6%	17.4%	16.4%	17.7%
Disposition						
Home	9.5%	16.9%	8.5%	36.4%	30.2%	38.1%
Short-term hospital	4.6%	3.0%	4.9%	4.2%	4.2%	4.2%
SNF	50.2%	37.3%	51.9%	31.1%	36.1%	29.7%
Home health	33.9%	40.6%	33.0%	27.3%	27.8%	27.2%
AMA	0.5%	2.2%	0.3%	0.9%	1.7%	0.7%
Unknown destination	1.3%	0.0%	1.4%	0.0%	0.0%	0.0%
Cardiovascular comorbidities						
AF	37.6%	35.9%	37.9%	30.3%	32.2%	29.8%
CAD	57.6%	52.9%	58.2%	64.1%	64.1%	64.1%
CKD	54.8%	62.1%	53.8%	37.0%	46.3%	34.4%
CVA	13.8%	12.1%	14.0%	10.2%	11.3%	10.0%
DM	8.0%	9.7%	7.8%	11.1%	10.7%	11.2%
uncomplicated DM	33.4%	35.6%	33.1%	29.5%	36.4%	27.6%
complicated						
HTN	9.6%	6.4%	10.0%	19.0%	14.1%	20.3%
HLD	45.1%	43.0%	45.4%	50.9%	49.5%	51.2%
HF	85.3%	88.6%	84.9%	72.4%	80.3%	70.3%
HFpEF	10.0%	6.7%	10.4%	9.8%	11.4%	9.4%
Obesity	13.1%	17.4%	12.6%	20.4%	20.7%	20.4%
Pulmonary	25.6%	26.4%	25.5%	19.1%	22.2%	18.3%
HTN						
Valvular heart disease	10.9%	7.8%	11.4%	11.0%	11.2%	10.9%
Inpatient outcomes						
LOS (days)	14.6	17.9	14.1	15.0	17.0	14.4
Total hospital cost	\$51,083	\$60,793	\$50,290	\$66,815	\$73,089	\$68,010

Abbreviations: AF, atrial fibrillation/flutter; AMA, against medical advice; CAD, coronary artery disease; CKD, chronic kidney disease; CVA, cerebrovascular accident; DM, diabetes mellitus; DNR, do not resuscitate; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HLD, hyperlipidemia; Hosp, hospitalization; HTN, hypertension; LOS, length of stay; PCS, palliative care services; SNF, skilled nursing facility.

Values are median or percentage.

stay information, or having been discharged in the last month of observation (Fig. 1). There were 133,738 survey-weighted CS index admissions in 2017 in the United States, with a total inpatient mortality of 36.3%. Among those who survived, 8.6% of CS admissions used PCS and 21% were readmitted within 30 days. Among 26,951 CS with PCS index admissions, the inpatient mortality rate was 72.8%.

Among those who survived ($n = 7326$), 11.6% ($n = 850$) were readmitted within 30 days and 61.3% ($n = 4,493$) had DNR orders. Of 106,787 CS without PCS index admissions, 27% died inpatient. Among those who survived ($n = 77,882$), 21.9% ($n = 17,036$) were readmitted within 30 days and 7.3% ($n = 5712$) had DNR orders. The mean length of stay including those who died during the index

Table 2. Hospital Characteristics of Cohort Cardiogenic Shock Population, Stratified by PCS Use (Survey Weighted, Excluding Patients Who Died During the Index Admission)

Characteristics	PCS Group			Non-PCS Group		
	Overall (N = 7326)	Readmitted (n = 850)	Not readmitted (n = 6476)	Overall (N = 77,882)	Readmitted (n = 17,036)	Not readmitted (n = 60,846)
Bed size						
Small	9.4%	7.4%	9.7%	8.7%	8.9%	8.6%
Medium	23.8%	20.3%	24.3%	22.7%	22.3%	22.8%
Large	66.7%	72.3%	66.0%	68.6%	68.7%	68.6%
Teaching status						
Urban nonteaching	16.4%	13.6%	16.8%	16.2%	15.3%	16.5%
Urban teaching	80.0%	85.7%	79.3%	80.0%	81.3%	79.7%
Nonmetro	3.5%	0.7%	3.9%	3.7%	3.4%	3.8%
Ownership						
Government nonfederal	9.7%	11.2%	9.5%	10.6%	11.2%	10.4%
Private nonprofit	82.0%	83.8%	81.7%	78.2%	78.1%	78.2%
Private investment	8.3%	5.0%	8.7%	11.2%	10.8%	11.3%

Metro, metropolitan; PCS, palliative care services.

admission was 10.4 days for the PCS group and 12.9 days for the non-PCS group. The mean length of stay among those who survived was 14.6 days for the PCS group and 15.0 days for the non-PCS group. The most frequent discharge destination for the PCS group was a skilled nursing facility (SNF) (50.2%) and for the non-PCS group was home (36.4%). The average time to readmission was 11.8 days for both the PCS and the non-PCS groups. The

mean total cost per patient during index admission was \$51,083 ± \$2629 for the PCS group and \$66,815 ± \$1729 for the non-PCS group.

Etiologies of 30-Day Readmission

The most frequent etiologies of readmission in PCS group overall included heart failure (32.1%), septicemia

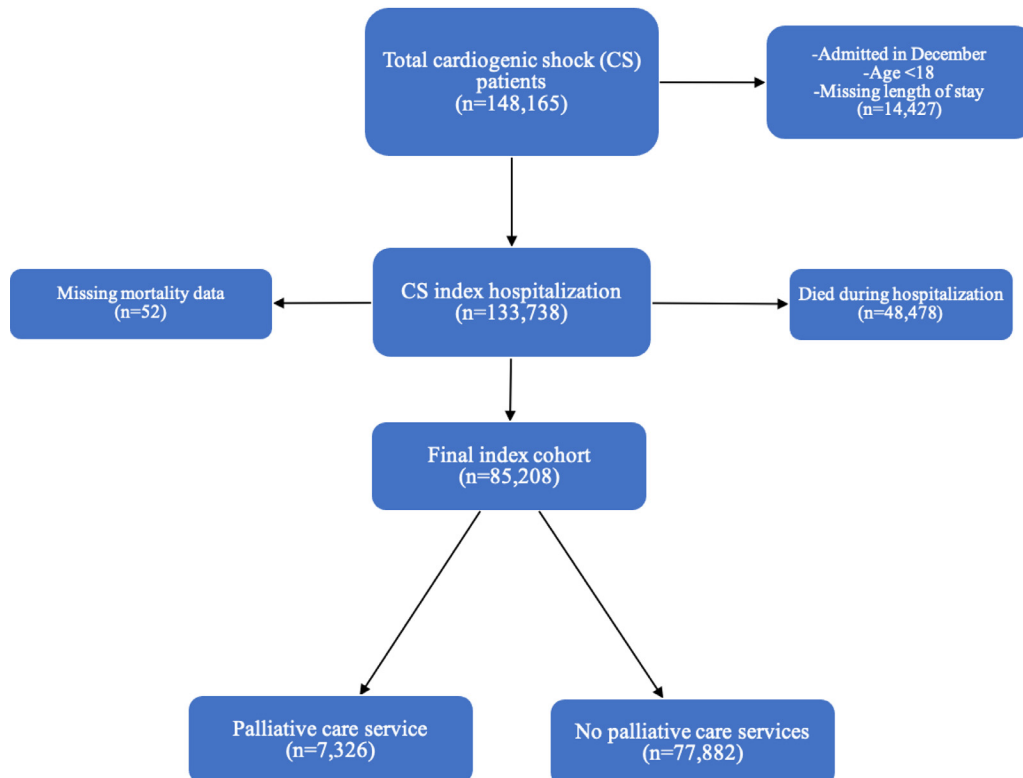


Fig. 1. Cohort population flow chart diagram (survey weighted).

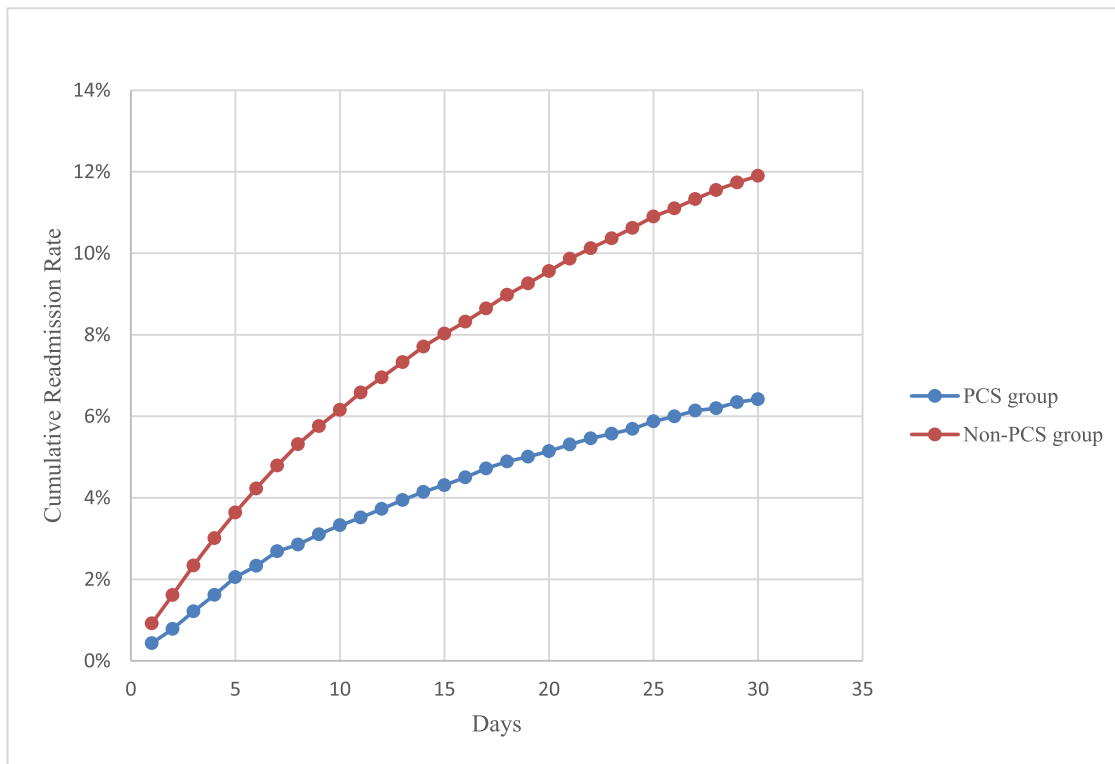


Fig. 2. Cumulative rate of first readmission among index population, stratified by palliative care services (PCS) vs non-PCS. *Cohort not limited to those readmitted within 30 days only.

(10.2%), and complication with a cardiovascular device, implant, or graft (4.2%). Cardiac etiologies of readmission consisted of 47.6% of all readmissions, followed by infectious (10.2%) and pulmonary (8.5%) etiologies (Fig. 3). The most common cardiac diagnoses of readmission were heart failure, cardiac arrhythmias, and AMI.

In the non-PCS group, the most common etiologies of readmission overall consisted of heart failure (24.4%), septicemia (9.1%), and cardiac arrhythmias (4.7%). Cardiac etiologies of readmission comprised 45.4% of all readmissions, followed by pulmonary (9.2%) and infectious (9.2%) etiologies (Fig. 3). The most common cardiac diagnoses of readmission were heart failure, cardiac arrhythmias, and AMI.

Predictors of 30-Day Readmission

PCS (OR 0.462, 95% CI 0.408–0.524, $P < .001$), DNR order (OR 0.679, 95% CI 0.606–0.761, $P < .001$), private pay (OR 0.763, 95% CI 0.710–0.820, $P < .001$), self-pay (OR 0.741, 95% CI 0.622–0.883, $P = .001$), and cardiac arrest (OR 0.809, 95% CI 0.728–0.899, $P < .001$) were independent predictors of lower 30-day readmission for all patients hospitalized with CS (Tables 3).

Discharges to a short-term hospital (OR 1.273, 95% CI 1.008–1.608, $P = .043$), SNF (OR 1.200, 95% CI 1.118–1.288, $P < .001$), and leaving against medical advice (OR 2.625, 95% CI 2.109–3.267, $P < .001$) were associated with a higher rate of 30-day readmission

(Table 3). Multiple chronic comorbidities were positive predictors of 30-day readmission: anemia (OR 1.126, 95% CI 1.066–1.189, $P < .001$), chronic kidney disease (OR 1.296, 95% CI 1.217–1.379, $P < .001$), cirrhosis (OR 1.159, 95% CI 1.007–1.334, $P = .040$), diabetes mellitus (OR 1.133, 95% CI 1.047–1.227, $P = .002$), diabetes mellitus with complications (OR 1.239, 95% CI 1.170–1.313, $P < .001$), congestive heart failure (OR 1.357, 95% CI 1.261–1.460, $P < .001$), and a history of ventricular tachycardia (OR 1.109, 95% CI 1.040–1.182, $P = .002$). Dialysis was associated with higher 30-day readmission (OR 1.283, 95% CI 1.125–1.464, $P < .001$), whereas multiple invasive procedures such as intubation, Impella, right heart catheterization, percutaneous coronary intervention, and placement of peripheral ventricular assist device were not significant predictors of 30-day readmission (Tables 3 and Supplementary Table 2).

In the CS with PCS group, discharge to a SNF was a predictor of lower 30-day readmission, but was a predictor of higher 30-day readmission in the CS without PCS group (Supplementary Table 3). The CS with PCS group also had fewer comorbidities and procedures that were predictors of 30-day readmission compared with the CS without PCS group (Supplementary Table 3).

Discussion

This study of the NRD 2017 database found inpatient mortality rates of approximately 36%, readmission rates of

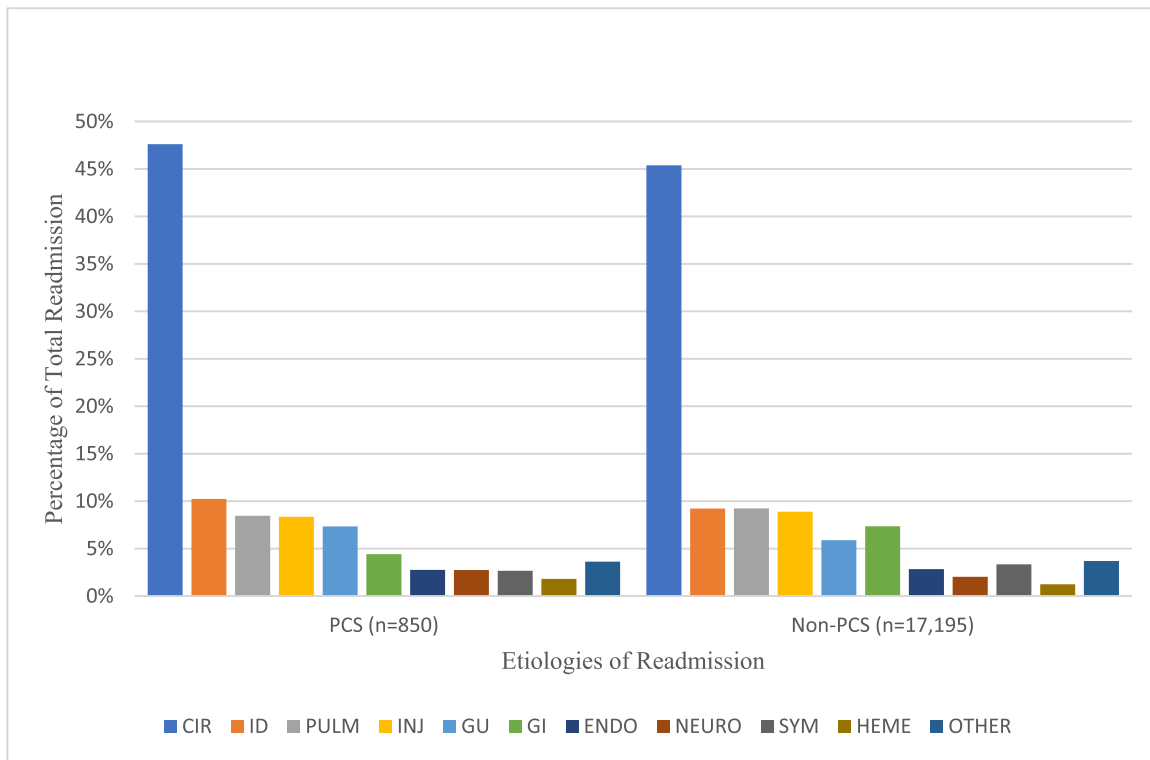


Fig. 3. Primary diagnoses for 30-day readmission in patients with cardiogenic shock (CS) with and without PCS (survey weighted). CIR, cardiovascular/circulatory; ENDO, endocrine, nutritional and metabolic; GI, digestive/gastroenterology; GU, genitourinary; HEM, hematologic; ID, infectious diseases; INJ, injury and poisoning; NEURO, nervous system; PCS, palliative care services; PULM, respiratory; SYM, symptoms, signs and abnormal clinical and laboratory findings; OTHER, includes dermatologic, mental/behavioral, neoplasms musculoskeletal, and ophthalmologic diseases.

approximately 21%, mean total hospitalization costs of approximately \$66,000, and a use of PCS of approximately 8.6%. Vallabhajosyula et al⁴ had also identified PCS under-use and similar independent predictors of PCS using the National Inpatient Sample for the CS complicating AMI population; however, our study is the first observational study to use a large readmission database to provide valuable readmission predictors and outcomes in all patients hospitalized with CS, regardless of AMI status.

Although we identified that PCS during the index admission for CS was associated with higher inpatient mortality compared with those without PCS (72.8% vs 27.0%), PCS was associated with significantly lower rates of readmission (11.6% vs 21.9%) and total hospitalization costs (\$51,083 ± \$2629 vs \$66,815 ± \$1729) despite a similar length of stay (14.6 vs 15 days) compared with those without PCS during index admission. This finding may be explained by detailed discussions of prognosis and advanced planning with the palliative care team resulting in changes in patients' goals of care toward less aggressive measures and/or hospice care after discharge.²¹ In the readmitted cohort, those who received PCS during index hospitalization had a similar length of stay compared with those who did not receive PCS (17.9 vs 17.0 days), but total the readmission costs remained lower for those who received PCS (\$60,793 ± 3939 vs \$73,089 ± 2162). A decrease in life-sustaining

and organ support therapies during hospitalization may account at least in part for these findings.

Among patients who survived the initial hospitalization, the main cause of readmission was heart failure regardless of the use of PCS. Heart failure readmission make up a greater proportion of readmissions in those receiving PCS compared with those without PCS during index admission, suggesting a high importance of close follow-up with a multidisciplinary team, including cardiologists and the palliative care team after discharge.

We identified multiple conditions associated with higher rates of 30-day readmission. The non-PCS group had more comorbidities that were predictors of higher readmission compared with the PCS group (Supplementary Table 3), suggesting the possibility that PCS mitigates the risk of readmission related to many of the comorbidities, helps to improve communication, and allows an easier transition to palliative and comfort care measures when appropriate. Approximately one-half of the patients in the PCS group and one-third of the non-PCS group were discharged to a SNF. However, discharge to a SNF was a predictor of lower readmission for the PCS group, in contrast with being a predictor of higher readmission rates for the non-PCS group (Supplementary Table 3). This finding may be explained by a transition to palliative care and/or hospice upon discharge to a SNF, leading to fewer readmissions.

Table 3. Predictors of 30-Day Readmission in the Cohort Cardiogenic Shock Population

Predictors	Odds Ratio	95% Confidence Interval	P Value
Palliative care services	0.462	0.408–0.524	<.001
Age	0.996	0.994–0.999	.002
DNR status	0.679	0.606–0.761	<.001
Female	1.070	1.014–1.130	.015
Insurance			
Medicare	Ref		
Private	0.763	0.710–0.820	<.001
Self-pay	0.741	0.622–0.883	.001
Other	0.712	0.610–0.832	<.001
Disposition			
Home	Ref		
Short-term hospital	1.273	1.008–1.608	.043
SNF	1.200	1.118–1.288	<.001
AMA	2.625	2.109–3.267	<.001
Comorbidities			
Anemia	1.126	1.066–1.189	<.001
Cardiac arrest	0.809	0.728–0.899	<.001
CKD	1.296	1.217–1.379	<.001
Cirrhosis	1.159	1.007–1.334	.040
DM	1.133	1.047–1.227	.002
DM with complications	1.239	1.170–1.313	<.001
HF	1.357	1.261–1.460	<.001
VT	1.109	1.040–1.182	.002
Procedures			
Dialysis	1.283	1.125–1.464	<.001

The length of stay was significant modeled as $1/x + 1/x^2$ under multivariable fractional polynomial.

AMA, against medical advice; CKD, chronic kidney disease; DM, diabetes mellitus; DNR, do not resuscitate; HF, heart failure; LHC, left heart catheterization; SNF, skilled nursing facility; VT, ventricular tachycardia.

The model is adjusted for health insurance, income, hospital characteristics, and comorbidities.

*Multivariate logistic regression model accounting for the Nationwide Readmissions Database survey structure was used to evaluate predictors of 30-day readmission events. Length of stay had a curvilinear relationship and was modeled using multivariable fractional polynomials as $\frac{1}{x} + \frac{1}{x^2}$.

PCS and DNR status are both independent predictors for lower 30-day readmission rates among all patients hospitalized with CS. However, 61.3% of the PCS group had DNR orders compared with only 7.3% of the non-PCS group, thus, further highlighting the need for inpatient consultation to palliative care team in this vulnerable cohort. Warraich et al²² suggested the incorporation of early goals of care discussions and palliative care to identify patients with contraindication to escalation of interventions or unwillingness to undergo aggressive care as part of the CS approach. The findings from our study help to strengthen this shared decision-making approach to CS by emphasizing the benefits of PCS in conforming goals of care and in decreasing the care burden for patients and society. Other predictors of lower 30-day readmission included private pay and self-pay. This finding indicates differences in patient demographics; socioeconomic status likely led to discrepancy in outcomes in patients hospitalized with CS. We were only able to adjust for readmission factors based on income quartile data because the NRD does not include information on level of education, race, or ethnicity.

This study uses the largest all-payer readmission database to assess outcomes on PCS use in CS hospitalizations. The study is limited by its observational retrospective database. The database also does not include information on out-of-hospital deaths after discharge, which will influence readmission risk. Readmissions are not tracked across calendar years and administrative errors including inaccurate data entry, inaccurate coding, and the inability to completely capture inpatient use of PCS in NRD may also occur. We acknowledge that using ICD-10 codes may underestimate the ability to capture PCS from administrative hospital data. Other limitations include the possibility that patients may have already been followed by a palliative care team in the outpatient setting, resulting in an easy transition to hospice care in the inpatient setting. Further stratification of results based on etiologies of CS (AMI, acute decompensated heart failure, postcardiotomy) may provide further insight into differences in outcomes in future studies with a larger cohort. The findings in our study are hypothesis generating and future prospective randomized studies are needed to confirm benefits of PCS in this vulnerable population.

In conclusion, the use of PCS in patient who survived a CS admission remains low at approximately 8.6% in 2017. Those receiving PCS during index admission had lower readmission rates and hospitalization costs than those without PCS. PCS and DNR orders were associated with lower rates of 30-day readmissions. PCS are associated with a decrease in future acute care service use for critically ill cardiac patients and are underused for high-risk cardiac patients.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.cardfail.2021.01.020](https://doi.org/10.1016/j.cardfail.2021.01.020).

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