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Original Article

Need for Support: Facilitating Early Transfer of Cardiogenic Shock Patients to Advanced Heart Failure Centres

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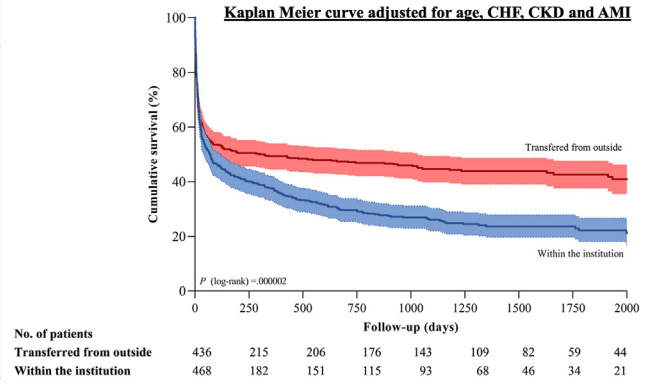
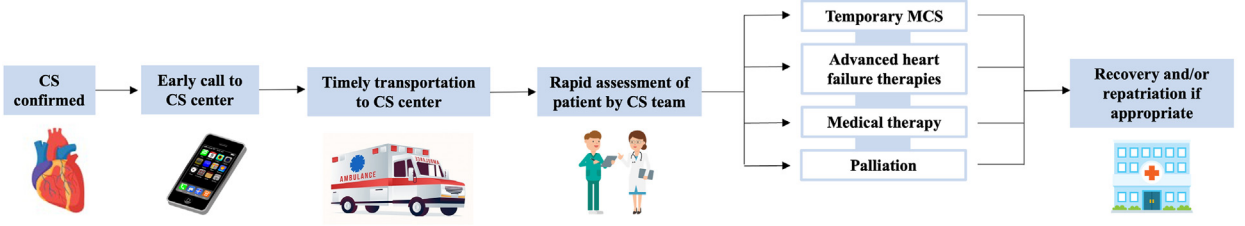
Characteristic	Admitted from within institution (n=476)	Transfer from outside hospital (n=440)
Age, years	63.3±16.3	56.5±14.7
Interventions in CICU		
Mechanical ventilation	↓	↑
IABP	↓	↑
Impella	↓	↑
ECLS	↓	↑
Durable LVAD	↑	↓
Heart transplant	↑	↓
Hospital length of stay, days	21 (10-38)	12 (5-22)
All-cause mortality at follow-up	299 (62.8%)	230 (52.3%)





ABSTRACT

Background: Cardiogenic shock (CS) is a complex, life-threatening condition that requires timely care of patients. The purpose of this study is to evaluate the characteristics and outcomes of patients transferred to a cardiac intensive-care unit from outside hospitals, compared to those of patients admitted directly to a CS centre.

Methods: Patients admitted with CS (January 1, 2014-December 31, 2019) were analyzed. Clinical characteristics and outcomes were recorded.

RÉSUMÉ

Contexte : Le choc cardiogénique (CC) est une condition complexe qui met en jeu le pronostic vital et qui nécessite une prise en charge rapide des patients. L'objectif de cette étude est d'évaluer les caractéristiques et les pronostics des patients transférés dans une unité de soins intensifs cardiaques à partir d'hôpitaux extérieurs, par rapport à ceux des patients admis directement dans un centre spécialisé en CC.

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Results: A total of 916 patients were admitted with CS; 440 (48.0%) were transferred from outside hospitals, and 476 (52.0%) were admitted directly to our institution. Transferred patients were younger (56.5 ± 14.7 vs 63.3 ± 16.3 years, $P < 0.001$), required vasopressor support more often (63.6% vs 14.9%, $P < 0.001$), and required mechanical ventilation more often (40.6% vs 10.7%, $P < 0.001$) upon transfer to the cardiac intensive-care unit. Transferred patients more frequently required extracorporeal life support (8.9% vs 3.0%, $P < 0.001$), had a lower rate of requiring orthotopic heart transplantation (6.4% vs 14.6%, $P < 0.001$), and had a lower incidence of all-cause mortality during follow-up (52.3% vs 62.8%, $P = 0.001$). With a multivariate analysis, patients transferred from outside were found to be less likely to reach the composite endpoint of durable ventricular assist device, orthotopic heart transplantation, or death (hazard ratio 0.75, 95% confidence interval 0.62-0.90, $P = 0.003$).

Conclusions: Marked differences are present in the characteristics and outcomes of patients transferred from outside institutions vs of those transferred from within our quaternary-care centre. Further studies are required to evaluate decision-making for transfer of CS patients and assess CS outcomes in the setting of standardized CS protocols and interventions.

Méthodes : Les données des patients admis pour un CC (entre le 1er janvier 2014 et le 31 décembre 2019) ont été analysées. Les caractéristiques cliniques et les pronostics ont été enregistrés.

Résultats : Au total, 916 patients ont été admis pour un CC; 440 (48,0 %) ont été transférés d'hôpitaux extérieurs et 476 (52,0 %) ont été admis directement dans notre établissement. Les patients transférés étaient plus jeunes (56,5 ± 14,7 vs 63,3 ± 16,3 ans, $p < 0,001$), nécessitaient plus souvent un soutien vasopresseur (63,6 % vs 14,9 %, $p < 0,001$) et plus souvent une ventilation mécanique (40,6 % vs 10,7 %, $p < 0,001$) lors de leur transfert à l'unité de soins intensifs cardiaques. Ces patients avaient aussi plus souvent besoin d'une assistance cardiorespiratoire extracorporelle (8,9 % vs 3,0 %, $p < 0,001$), avaient moins souvent besoin d'une transplantation cardiaque orthotopique (6,4 % vs 14,6 %, $p < 0,001$) et présentaient une incidence plus faible de mortalité toutes causes confondues lors du suivi (52,3 % vs 62,8 %, $p = 0,001$). Une analyse multivariée a montré que les patients transférés de l'extérieur étaient moins susceptibles d'atteindre le critère d'évaluation composite (dispositif d'assistance ventriculaire durable, transplantation cardiaque orthotopique ou décès) (rapport de risque 0,75, intervalle de confiance à 95 % 0,62-0,90, $p = 0,003$).

Conclusions : Des différences marquées sont présentes dans les caractéristiques et les pronostics des patients transférés depuis des institutions extérieures par rapport à ceux admis directement dans notre centre de soins quaternaires. Des études supplémentaires sont nécessaires pour évaluer la prise de décision concernant le transfert des patients atteints de CC et évaluer les pronostics de la CC dans le cadre de protocoles et d'interventions de CC standardisés.

Cardiogenic shock (CS) is a low-cardiac-output state with life-threatening end-organ hypoperfusion and hypoxia associated with significant morbidity and mortality.[1] CS can occur as a result of acute myocardial infarctions (AMI), acute exacerbation of chronic heart failure (CHF), and<!–Q3: AU: CHF is defined as both chronic heart failure and congestive heart failure— adjust to clarify–> other nonischemic etiologies, including severe valvular disease and myocarditis. These patients generally are admitted to cardiac intensive-care units (CICUs) for aggressive medical management and are evaluated for advanced therapies in specialized centres, including mechanical circulatory support (MCS) and orthotopic heart transplantation (OHT).

A common cause of CS is AMI. The **SH**ould We Emergently Revascularize **O**ccluded Coronaries for **C**ardiogenic Shoc**K** (SHOCK) trial noted that urgent revascularization in patients with AMI improved the survival rate in those with CS.[2] Subsequent guidelines from the American Heart Association (AHA) also highlight the importance of transferring patients with ST-elevation myocardial infarction with CS to facilities capable of cardiac catheterization with rapid revascularization,[3] which is associated with a reduction in 1-year mortality rates (81.9% before 1999 vs 71.5% after 2004).[4] Although most CS studies have been completed in the AMI population, a contemporary analysis of patients admitted to the hospital with non-AMI CS found similar rates of in-hospital mortality[5] and highlighted the need to understand how we can improve outcomes for all those with CS. <!–Q4: AU: In sentence beginning "Although most CS" —is "all those with CS" correct as edited? Or provide alternative specification of "all-comers"— all those admitted to the hospital?–>

As clinical practice patterns have significant variations, recommendations have been proposed by the AHA to streamline care, build new infrastructure through CS algorithms, and develop dedicated CS centres,[1] which can improve the outcomes of patients with heart failure (HF)[6] by potentially enabling timely access at select centres specializing in advanced HF therapies. In addition, a novel classification of CS, developed by the Society for Cardiovascular Angiography and Interventions (SCAI) that describes disease severity can assist in its early identification and triage,[7] and in some studies, it can assist in the selection of a subset of patients who warrant assessment for advanced therapies.[8]

The University Health Network's Peter Munk Cardiac Centre at Toronto General Hospital is a quaternary-care centre that acts as 1 of 3 provincial hubs for advanced HF care, providing durable mechanical circulatory support and cardiac transplant services to more than 6 million Canadian adults.[9] The centre provides care for patients with complex cardiovascular conditions, including CS, in the CICU, both those from the local population of patients who are admitted

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See page 1350 for disclosure information.

directly to the institution and those transferred from outside hospitals. This study compares patients with CS and their outcomes, for those transferred to the CICU from outside hospitals vs those admitted directly to a CS centre.

Methods

Study design

All adult patients admitted with CS to the CICU between January 1, 2014 and December 31, 2019 were identified from a prospective database of all admissions. The diagnosis of CS was made by the treating physician utilizing the following criteria from the SHOCK trial[2] and the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP SHOCK II) [10] trial: clinical criteria of systolic blood pressure of < 90 mm Hg for ≥ 30 minutes or a requirement for vasopressors or inotropes to maintain systolic blood pressure at ≥ 90 mm Hg); pulmonary congestion; evidence of end-organ hypoperfusion (altered mental status, cool extremities, urine output < 30 cc/h, lactate > 2 mmol/L), or hemodynamic criteria of cardiac index of ≤ 2.2 L/min/m^2 and pulmonary capillary wedge pressure of ≥ 15 mm Hg). Data were abstracted through clinical review of the patient's electronic medical record, including their admission diagnosis, and corroborated by their clinical notes. All clinical data were retrieved from the CICU registry for each patient's index admission to the CICU during their hospital stay. If a patient had > 1 CICU admission during their hospital stay, only the index CICU admission was included in our analysis. Patients with a previous history of OHT or a left ventricular assist device (LVAD) were excluded from the study.

Patients were admitted to the CICU from the institution's emergency departments, inpatient ward, other critical-care units, or were transferred from other hospitals for specialized care. Data on clinical characteristics, admission laboratory values (at the time of admission or the first value recorded during CICU admission within the first 24 hours), interventions received while in the CICU, as well as discharge medications, clinical follow-up, CICU and hospital length-of-stay, and receipt of either temporary or durable MCS and/or OHT were extracted. Patient location prior to CICU admission was recorded, as well as concurrent diagnoses, including AMI, non-AMI-related acute decompensated heart failure (ADHF), arrhythmia, postcardiac arrest, and sepsis. Mortality rates (with a follow-up period lasting up to May 31, 2021) were recorded. The University Health Network research ethics board review committee approved this study.

Outcomes

The following outcomes were included: all-cause mortality at the time of follow-up, durable LVAD implantation or OHT at the time of follow-up, in-hospital mortality, 30-day mortality from the time of CICU admission, and a composite endpoint consisting of durable LVAD implantation, OHT, or all-cause mortality at the time of follow-up. The latter endpoint was analyzed with censoring of the follow-up at the time a patient received an LVAD implant or OHT; the endpoint was used, as it encompassed the most-severe shock states, with the consideration that without OHT or durable MCS, patients with CS likely would have died.

Statistical analysis

Categorical variables are presented as proportion (percentage), and continuous variables are summarized by mean $\pm$ standard deviation (SD) or median (25th-75th percentile). Proportions of categorical variables were compared using the χ^2 test, and the Fisher exact probability test was used when data were limited. Means for continuous variables were compared using t-tests for dichotomous variables, ANOVA tests (general linear model) for categorized variables when the data were normally distributed, and the Mann-Whitney U test when data were non-normally distributed. Standardized mean differences (SMDs) in baseline characteristics between groups were determined using Cohen's d for continuous data; Phi was calculated for categorical data; and Cramér's V was used for variables with more than 2 levels (such as SCAI stage). Kaplan-Meier analysis and the log-rank test were used to evaluate and compare event-free survival between patients transferred to the CICU from outside hospitals and those who were admitted to the CICU from within the institution. In addition, multivariate Cox proportional-hazards models were adjusted for clinically important variables (age, sex, history of congestive heart failure (CHF), previous myocardial infarction, acute coronary syndrome, post—cardiac arrest, hypertension, dyslipidemia, diabetes mellitus, admission hemoglobin levels, admission serum sodium concentration, peripheral vascular disease, chronic kidney disease, smoking status, admission lactate, ventricular tachycardia and/or ventricular fibrillation, atrial fibrillation or flutter, vasopressor use, mechanical ventilation, intra-aortic balloon pump (IABP) or Impella (Abiomed/Johnson & Johnson, Danvers, MA) pump use, and pulmonary artery catheter use). These models were used to examine the association of transfer group and all-cause mortality; durable LVAD implantation or OHT; as well as the association between transfer group and in-hospital mortality, 30-day mortality from the time of CICU admission.

An additional sensitivity analysis was performed using propensity-score matching, with values imputed (ie, median lactate) when they were missing in matched samples, using a caliper width of 0.2 of the standard deviation of the logit of the propensity score. (Supplemental Table S1).

All statistical tests were 2-sided, and a $P < 0.05$ was deemed to be statistically significant. Standardized differences of 0.2, 0.5, and 0.8 were used to determine small, medium, and large differences between the populations, respectively. Statistical analyses were performed using SPSS software, version 29.0.0.1 (IBM, New York, NY). The authors are solely responsible for the design and conduct of this study, its analysis, the drafting and editing of this paper, and its final contents.

Results

Patient characteristics

During the study period, 916 patients were admitted to the CICU with a diagnosis of CS. The mean age of these patients was 60 years, and 641 (70%) were male. A total of 440 patients (48.0%) were transferred from outside hospitals, and

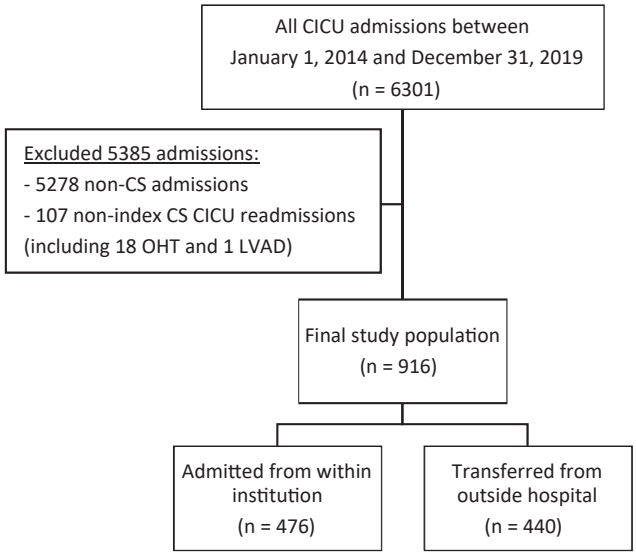

Figure 1. Study inclusion and exclusion criteria, and study populations either admitted from within institution or transferred from outside hospitals. CICU, cardiac intensive-care unit; CS, cardiogenic shock; OHT, orthotopic heart transplantation; LVAD, left ventricular assist device.

476 (52.0%) were admitted directly from our institution (Fig. 1).

The patients who were transferred in were younger (56.5 vs 63.3, SMD 0.44, $P < 0.001$), and they were less likely to have a previous history of CHF (37.9% vs 62.7%, SMD 0.25, $P < 0.001$), coronary artery bypass grafting (6.4% vs 13.5%, SMD 0.12, $P < 0.001$), or adult congenital heart disease (3.3% vs 6.4%, SMD 0.07, $P = 0.04$), compared to those admitted from within the institution (Table 1). Those transferred from outside had lower rates of comorbid illnesses, including atrial fibrillation or flutter, ventricular tachycardia or fibrillation, and chronic kidney disease; they were more likely to be a smoker at the time of admission and less likely to have an implantable cardioverter defibrillator or cardiac resynchronization therapy—defibrillator. They also were less likely to be on guideline-directed medical therapies for the treatment of HF, in keeping with the lower incidence of a previous history of CHF in this group.

No significant differences occurred in the proportion of patients transferred for AMI-CS (23.0% vs 19.3%, $P = 0.52$) and ADHF-CS (77.1% vs 80.7%, $P = 0.10$) vs the proportion admitted directly to our institution. Higher heart rates were noted in those transferred (96.6 ± 21.9 vs 85.0 ± 22.1, SMD 0.66, $P < 0.001$); however, the mean arterial pressure was similar. Patients who were transferred in to the CICU had more critical-care interventions, including vasopressor support (63.6% vs 14.9%, SMD 0.50, $P < 0.001$), mechanical ventilation (40.6% vs 10.7%, SMD 0.34, $P < 0.001$), intra-aortic balloon pump (IABP) or Impella use (21.8% vs 4.4%, SMD 0.26, $P < 0.001$), and pulmonary artery catheters for hemodynamic monitoring (3.9% vs 0.6%, SMD 0.11, $P < 0.001$), compared to those directly admitted to the CICU within the institution. Despite this difference, vasopressor use during the CICU admission was not significantly different statistically between the 2 groups. Laboratory values at admission, including levels of creatinine, brain natriuretic peptide, and serum lactate, were also similar.

Using retrospectively determined SCAI-CS classification, stratified based upon drug and device utilization,[7,11] the majority of patients at the time of CICU admission were in stage D of the disease (n = 805; 87.9%), with no differences noted between the 2 study groups. During their CICU admission, patients who were transferred from outside centres continued to require higher rates of use, compared with those admitted directly, of mechanical ventilation (44.8% vs 23.5%, $P < 0.001$), IABP (23.6% vs 11.8%, $P < 0.001$), pulmonary artery catheter (54.8% vs 38.7%, $P < 0.001$), as well as Impella device support (4.1% vs 1.9%, $P = 0.049$; Table 2; graphical abstract). They also were more likely to require use of renal replacement therapy (RRT; 13.5% vs 17.9%, $P < 0.001$).

Advanced therapies and outcomes

With respect to advanced HF therapies (Table 3; graphical abstract), patients who were transferred, compared to those admitted directly, were more likely to require extracorporeal life support (ECLS; 8.9% vs 3.0%, $P = < 0.001$) during their hospital admission. No significant difference occurred between the 2 groups with respect to the use of durable LVAD (9.9% of those transferred vs 13.7% of those admitted from within the institution, $P = 0.08$), but patients who were transferred in were less likely to receive an OHT (6.4% vs 14.6%, $P < 0.001$).

The CICU length-of-stay was similar between the 2 groups, but those transferred in had a significantly shorter length of hospital stay, compared to that of those admitted from within our institution (12 days (IQR 5-22) vs 21 days (IQR 10-38), $P < 0.001$). The rates of in-hospital mortality (32.5% vs 33.8%, $P = 0.67$) and 30-day mortality from time of CICU admission (9.1% vs 9.0%, $P = 0.99$) were not significantly different statistically between the 2 groups. However, at the time of last follow-up (May 31, 2021; follow-up range of 0.41-7.42 years), the mortality rate was increased

Table 1. Baseline characteristics and admissions data

Characteristics	All patients (n = 916)	Admitted from within institution (n = 476)	Transferred from outside hospital (n = 440)	SMD	*P*
Age, y	60.0 ± 15.9	63.3 ± 16.3	56.5 ± 14.7	0.44	< 0.001
Male sex	641 (70.0)	328 (68.9)	313 (71.1)	0.02	0.46
Comorbidities					
Hypertension	402 (44.0)	220 (46.2)	182 (41.6)	−0.05	0.16
Dyslipidemia	319 (34.8)	179 (37.6)	140 (31.8)	−0.06	0.066
Diabetes	295 (32.2)	160 (33.6)	135 (30.7)	−0.03	0.34
Previous MI	192 (21.0)	103 (21.6)	89 (20.2)	−0.02	0.60
Previous PCI	152 (16.6)	83 (17.4)	69 (15.7)	−0.02	0.48
Previous CABG	92 (10.0)	64 (13.5)	28 (6.4)	−0.12	< 0.001
Chronic kidney disease	240 (26.3)	164 (34.5)	76 (17.3)	−0.20	< 0.001
Cerebrovascular accident	87 (9.5)	52 (10.9)	35 (8.0)	−0.05	0.13
Peripheral vascular disease	55 (6.0)	35 (7.4)	20 (4.6)	−0.06	0.07
Previous history of CHF	464 (50.8)	298 (62.7)	166 (37.9)	−0.25	< 0.001
Previous history of VT and/or VF	90 (9.8)	62 (13.1)	28 (6.4)	−0.11	< 0.001
Previous history of atrial fibrillation and/or flutter	273 (29.9)	184 (38.7)	89 (20.3)	−0.20	< 0.001
Presence of permanent pacemaker	39 (4.3)	25 (5.3)	14 (3.2)	−0.05	0.12
Presence of ICD	239 (25.8)	157 (33.0)	79 (18.0)	−0.17	< 0.001
Presence of CRT-D	103 (11.3)	73 (15.4)	30 (6.8)	−0.14	< 0.001
Chronic obstructive pulmonary disease	64 (7.0)	31 (6.5)	33 (7.5)	−0.02	0.55
Smoking history	272 (29.7)	122 (25.6)	150 (34.1)	0.14	0.005
History of ACHD	39 (5.0)	27 (6.4)	12 (3.3)	−0.07	0.04
Admission diagnosis					
AMI-CS	193 (21.1)	92 (19.3)	101 (23.0)		0.52
STEMI	136 (14.9)	68 (14.3)	68 (15.5)	0.02	0.62
NSTEMI/UA	57 (6.2)	24 (5.0)	33 (7.5)	0.05	0.12
ADHF-CS	727 (79.0)	385 (80.7)	342 (77.1)	−0.04	0.10
Arrhythmia	27 (3.0)	12 (2.5)	15 (3.4)	0.03	0.43
Sepsis	7 (0.8)	4 (0.8)	3 (0.7)	−0.01	1.0
Post−cardiac arrest	62 (6.8)	25 (5.3)	37 (8.4)	0.06	0.057
Admission laboratory values					
Hemoglobin, g/L	120.6 ± 25.3	118.9 ± 25.0	122.4 ± 25.5	−0.27	0.04
Platelet, 10^9/L	204.6 ± 94.8	199.9 ± 90.6	209.5 ± 98.8	−0.23	0.13
Sodium, mmol/L	134.9 ± 5.9	134.3 ± 5.4	135.5 ± 6.3	−0.32	0.004
Creatinine, umol/L	157 (106−243)	163 (111−246)	150 (101−238)	−0.05	0.24
Brain natriuretic peptide	1642 (811−2842)	1591 (907−3196)	1656 (705−2757)	−0.26	0.98
Serum lactate	2.2 (1.7−3.4)	2.2 (1.8−3.2)	2.2 (1.5−4.0)	−0.29	0.01
Admission vital signs					
Heart rate, bpm	90.6 ± 22.7	85.0 ± 22.1	96.6 ± 21.9	−0.66	< 0.001
MAP, mm Hg	75.1 ± 14.1	74.9 ± 14.9	75.3 ± 13.3	−0.03	0.63
Interventions pre-CICU admission					
Vasopressor use	350 (38.3)	71 (14.9)	279 (63.6)	0.50	< 0.001
Mechanical ventilation	229 (25.0)	51 (10.7)	178 (40.6)	0.34	< 0.001
BIPAP	18 (2.0)	6 (1.3)	12 (2.7)	0.05	0.11
IABP/Impella	117 (12.8)	21 (4.4)	96 (21.8)	0.26	< 0.001
IHD/PD	33 (3.6)	15 (3.2)	18 (4.1)	0.03	0.44
PA catheter	20 (2.2)	3 (0.6)	17 (3.9)	0.11	< 0.001
SCAI stage				0.04	0.66
B	59 (6.4)	30 (6.3)	29 (6.6)		
C	45 (4.9)	24 (5.0)	21 (4.8)		
D	805 (87.9)	422 (88.2)	385 (87.5)		
E	7 (0.8)	2 (0.4)	5 (1.1)		
Admission medications					
ASA	291 (31.8)	144 (30.3)	147 (33.4)	0.03	0.32
Thienopyridine	115 (12.6)	48 (10.1)	67 (15.3)	0.08	0.02
Beta-blocker	484 (52.8)	307 (64.5)	177 (40.2)	**−0.24**	< 0.001
ACEi/ARB	326 (35.6)	190 (39.9)	136 (30.9)	−0.09	0.004
Sacubitril and/or valsartan	33 (3.6)	19 (4.0)	14 (3.2)	−0.02	0.51
Aldosterone receptor antagonist	291 (31.8)	187 (39.4)	104 (23.6)	−0.17	< 0.001
Calcium-channel blocker	64 (7.0)	35 (7.4)	29 (6.6)	−0.02	0.65
Loop diuretic	456 (49.8)	298 (62.6)	158 (35.9)	**−0.27**	< 0.001
Hydralazine	82 (9.0)	61 (12.8)	21 (4.8)	−0.14	< 0.001
Nitrates	54 (5.9)	39 (8.2)	15 (3.4)	−0.10	0.002
Digoxin	159 (17.4)	114 (24.0)	45 (10.2)	−0.18	< 0.001

Table 1. Continued.

Characteristics	All patients (n = 916)	Admitted from within institution (n = 476)	Transferred from outside hospital (n = 440)	SMD	*P*
Statin	368 (40.2)	213 (44.8)	155 (35.2)	−0.10	0.003
Insulin	80 (8.7)	47 (9.9)	33 (7.5)	−0.04	0.20
Anticoagulation	199 (21.7)	122 (25.6)	77 (17.5)	−0.10	0.003

Values are n (%), mean ± standard deviation, or median (interquartile range), unless otherwise indicated. Impella device (Abiomed/Johnson & Johnson, Danvers, MA).

ACEi, angiotensin-converting enzyme inhibitor; ACHD, adult congenital heart disease; ADHF-CS, acute decompensated heart failure cardiogenic shock; AMI-CS, acute myocardial infarction cardiogenic shock; ARB, angiotensin II receptor blocker; ASA, acetylsalicylic acid; BIPAP, bilevel positive airway pressure; bpm, beats per minute; CABG, coronary artery bypass graft; CHF, congestive heart failure; CICU, cardiac intensive-care unit; CRT-D, cardiac resynchronization therapy—defibrillator; IABP, intra-aortic balloon pump; ICD, implantable cardioverter defibrillator; IHD, intermittent hemodialysis; MAP, mean arterial pressure; MI, myocardial infarction; NSTEMI, non-ST-elevation MI; PA, pulmonary artery; PCI, percutaneous coronary intervention; PD, peritoneal dialysis; SCAI, Society for Cardiovascular Angiography and Interventions; SMD, standardized mean difference; STEMI, ST-elevation myocardial infarction; UA, unstable angina; VF, ventricular fibrillation; VT, ventricular tachycardia.

in those admitted from within our institution (62.8% vs 52.3%, $P = 0.001$); this group also had a higher level of use of durable LVAD or OHT (19.7% vs 10.2%, $P < 0.001$; Table 3).

Univariate and multivariate analysis

Univariate analyses revealed a lower all-cause mortality rate in transferred patients, both when uncensored (hazard ratio [HR] 0.82, 95% confidence interval [CI] 0.69-0.97, $P = 0.02$) and when censored (HR 0.75, 95% CI 0.63-0.89, $P = 0.001$) at the time of LVAD or OHT; however, no difference occurred in the rates of in-hospital or 30-day mortality from the time of CICU admission. No difference occurred in the all-cause mortality rate, or the in-hospital or 30-day mortality from the time of CICU admission rate, noted in the multivariate analyses. For the advanced HF therapy requirement (durable LVAD or OHT) at the time of last follow-up, univariate analysis demonstrated that a lower rate of utilization occurred in transferred patients (HR 0.49, 95% CI 0.34-0.70, $P < 0.001$), which was no longer different in the multivariate analysis (HR 0.72, 95% CI 0.46-1.15, $P = 0.17$). The prespecified composite endpoint of LVAD, OHT, and all-cause mortality was lower in those transferred from outside hospitals at the time of follow-up (univariate analyses HR 0.69, 95% CI 0.59-0.81, $P < 0.001$, multivariate analyses HR 0.75, 95% CI 0.62-0.90, $P < 0.003$; Table 4). A total of 607 patients met the composite endpoint (251 transferred in from outside hospitals; 356 from within the institution).

Propensity-score matching was performed to control for clinically important variables, given the significant differences in baseline characteristics between the 2 groups. This additional analysis (n = 558) showed significant differences in all-cause mortality rate in both the univariate and multivariate analyses when censored at the time of LVAD or OHT. A reduction occurred in all-cause mortality, and a significantly lower composite endpoint occurred in patients who were transferred from outside institutions (Supplemental Table S1).

Population with CS, over time (2014-2016 vs 2017-2019)

A comparison of the population with CS, for different time periods, showed a notable increase in numbers of CS patients (Supplemental Table S2), with a total of 332 patients admitted with CS in the period 2014-2016 vs 577 in the period 2017-2019. However, no significant change occurred in the overall patient population, as patients transferred from outside hospitals continued to be younger, have lower rates of comorbid illnesses (including a previous history of CHF), and were more likely to require vasopressor use, mechanical ventilation, IABP and/or Impella use, and pulmonary artery catheter use prior to CICU admission. They also continued to have lower rates of use of guideline-directed medical therapy. Over time, an overall increase occurred in patients admitted for AMI-CS in both populations. Patients transferred from outside institutions had longer CICU stay—lengths but continued to have a shorter hospital length-of-stay, be less likely to require a ventricular assist device or OHT, and be more likely to need ECLS (Supplemental Table S3). A higher mortality rate continued in those admitted from within the institution at follow-up (Supplemental Table S4).

Discussion

Only a limited number of published reports describe the clinical characteristics and outcomes of CS patients transferred from outside hospitals, as compared to those for patients admitted directly to a specialist CS centre. In this analysis of patients admitted to a CICU, we found that those transferred from outside hospitals were younger, had fewer comorbidities, and had a *de novo* presentation of CHF. At the time of CICU presentation, these patients had an increased acuity and illness severity, leading to more aggressive intensive-unit care on admission, including vasopressor use, mechanical ventilation, and mechanical circulatory support (ECLS, IABP, or Impella support). No differences occurred in short-term outcomes, including in-hospital and 30-day mortality from the time of CICU admission (the latter used rather than 30-day mortality, as patients transferred will have spent a proportion of time postdischarge from our institution at the outside hospital to which they may have been readmitted). However, the incidence of the composite endpoint of LVAD, OHT, and all-cause mortality at the time of follow-up was lower in those transferred from outside hospitals. Overall, these mortality findings are similar to those for previous registries in AMI-CS,[12] and in a more recent study of CS network outcomes.[13]

This study highlights the significant differences in baseline characteristics in these 2 populations within our regional healthcare system. At the time of this study (2014-2019), standardized protocols for identification of CS and selection of

Table 2. Cardiac intensive-care unit (CICU) interventions

Characteristics	All patients (n = 916)	Admitted from within institution (n = 476)	Transferred from outside hospital (n = 440)	*P*
Interventions during CICU admission				
Vasopressor use	830 (90.6)	433 (91.0)	397 (90.2)	0.70
Dopamine use	66 (7.2)	27 (5.7)	39 (8.9)	0.06
Dobutamine use	267 (29.2)	124 (26.1)	143 (32.5)	0.03
Milrinone use	409 (44.7)	229 (48.1)	180 (41.0)	0.03
Mechanical ventilation	309 (33.7)	112 (23.5)	197 (44.8)	< 0.001
BIPAP	42 (4.6)	25 (5.3)	17 (3.9)	0.31
IABP	160 (17.5)	56 (11.8)	104 (23.6)	< 0.001
Impella	27 (3.0)	9 (1.9)	18 (4.1)	0.049
PA catheter	425 (46.4)	184 (38.7)	241 (54.8)	< 0.001
IHD	141 (15.6)	63 (13.5)	78 (17.9)	0.06

Impella device (Abiomed/Johnson & Johnson, Danvers, MA).

BIPAP, bilevel positive airway pressure; IABP, intra-aortic balloon pump; IHD, intermittent hemodialysis; PA, pulmonary artery.

patients for transfer were not available, as a citywide CS network had not been established. The recognition and identification of CS occurred at local hospitals, generally by emergency, internal medicine, or critical-care physicians and cardiologists. Once CS was recognized, individual physicians connected with the CS centre for transfer of care. Given this situation, variations occurred in decision-making, based upon individual provider choice at both the referring and receiving sites.

Studying the heterogeneous CS (AMI-CS and ADHF-CS) population is inherently difficult. Most studies have focused on AMI-CS in the era of transfer for revascularization, with variable outcomes. In a catheter-based LVAD registry study of revascularization and Impella devices, patients admitted directly to a tertiary-care centre were compared with those transferred from an outside hospital with AMI-CS.[14] The duration of CS pre-Impella insertion, and the mortality rate, in patients from a non-CS centre were similar (OR 0.91, 95% CI 0.59-1.38), compared to those for patients admitted directly to a CS centre. In contrast, a meta-analysis of Impella use in AMI-CS suggested that outcomes were improved (in-hospital and 30-day mortality from the time of CICU admission) with early initiation of MCS.[15] This finding has been evaluated further in a multicentre, randomized trial of ST elevation myocardial infarction−related CS patients that found a lower risk of death from any cause at 180 days with the use of the Impella CP plus standard care, compared to the risk with standard care alone (45.8% vs 58.5%, HR 0.74, $P = 0.04$).[16] Recently, the Cardiogenic Shock Working Group analyzed a contemporary cohort of CS patients (AMI-CS and HF-CS) and found that the mortality rate was higher in transferred patients (driven primarily by the HF-CS cohort), with higher age, and greater volume of critical-care interventions (mechanical ventilation, increased number of vasoactive medications), as well as RRT, being independent predictors of mortality in this population.[17]

To allow for earlier identification of CS and timely transfer of patients, standardized frameworks are needed, along with the development of CS networks within our regional health-care system. Implementation of strategies to identify patients, streamline transfer protocols, and create "shock teams" and "code shock" algorithms are required.[1] Through such implementation, hub and spoke centres can work together to ensure that patients receive timely and appropriate care at specialized centres. Since the release of an AHA scientific statement,[1] citywide networks have been formed. Tehrani et al.[13] have developed such a network with their hospital partners and have found that, irrespective of where the patients' index hospital was located, the incidences of risk-adjusted 30-day mortality and of the secondary endpoints of bleeding, stroke, and major adverse cardiovascular and cerebrovascular events were similar. Other sites have shown that a

Table 3. Discharge parameters, interventions, and mortality

Characteristics	All patients (n = 916)	Admitted from within institution (n = 476)	Transferred from outside hospital (n = 440)	*P*
Discharge parameters				
CICU LOS, d (range)	5 (2−9)	4 (2−8)	5 (2−10)	0.10
Hospital LOS, d (range)	16 (7−32)	21 (10−38)	12 (5−22)	< 0.001
In-hospital mortality	308 (33.6)	164 (34.5)	144 (32.7)	0.58
Interventions				
Postadmission durable LVAD	109 (11.9)	65 (13.7)	44 (9.9)	0.08
Postadmission transplant	97 (10.7)	69 (14.6)	28 (6.4)	< 0.001
ECLS	53 (5.8)	14 (3.0)	39 (8.9)	< 0.001
Durable LVAD or OHT up to May 2021	139 (15.2)	94 (19.7)	45 (10.2)	< 0.001
Mortality				
30-d	66 (9.1)	35 (9.0)	31 (9.1)	0.99
Up to May 2021	529 (57.8)	299 (62.8)	230 (52.3)	0.001

Values are n (%), unless otherwise indicated.

CICU, cardiac intensive-care unit; ECLS, extracorporeal life support; LOS, length of stay; LVAD, left ventricular assist device; OHT, orthotopic heart transplantation.

Table 4. Univariable and multivariable analysis of outcomes

	Uncensored			Censored at time of LVAD or OHT		
Variables	HR	95% CI	*P*	HR	95% CI	*P*
All-cause mortality						
Univariable, U	0.82	0.69−0.97	**0.02**	0.75	0.63−0.89	**0.001**
Multivariable, A*	0.86	0.70−1.05	0.14	0.82	0.67−1.01	0.06
Durable LVAD or OHT at last follow-up						
Univariable, U	0.49	0.34−0.70	**< 0.001**			
Multivariable, A*	0.72	0.46−1.15	0.17			
In-hospital mortality						
Univariable, U	1.09	0.87−1.36	0.47	1.07	0.85−1.34	0.58
Multivariable, A*	0.98	0.75−1.27	0.85	0.99	0.75−1.29	0.92
30-d mortality from time of CICU admission						
Univariable, U	1.05	0.84−1.32	0.66	1.02	0.82−1.29	0.84
Multivariable, A*	0.99	0.76−1.3	0.95	0.97	0.74−1.28	0.85
Composite endpoint (all-cause mortality, LVAD, OHT)						
Univariable, U	0.69	0.59−0.81	**< 0.001**			
Multivariable, A*	0.75	0.62−0.90	**0.003**			

Boldface indicates statistical significance. Univariate and multivariate analysis of all-cause mortality, durable left ventricular assist device (LVAD), or orthotopic heart transplantation (OHT), both at the time of follow-up; in-hospital mortality, 30-day mortality from time of cardiac intensive-care unit (CICU) admission (uncensored and censored at the time of LVAD or OHT), and composite endpoint (all-cause mortality, LVAD, or OHT) in those transferred from outside hospitals, compared to the same for those admitted from within the institution. Impella device (Abiomed/Johnson & Johnson, Danvers, MA).

A, adjusted; ACS, acute coronary syndrome; CHF, congestive heart failure; CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; IABP, intra-aortic balloon pump; MI, myocardial infarction; OHT, orthotopic heart transplantation; PVD, peripheral vascular disease; U, unadjusted; VF, ventricular fibrillation; VT, ventricular tachycardia.

*Adjusted for age, sex, CHF, previous MI, ACS, post−cardiac arrest, hypertension, dyslipidemia, diabetes mellitus, hemoglobin, sodium, PVD, CKD, smoking status, lactate (if missing, imputed with median value of 2.2 mmol/L), VT and/or VF, atrial fibrillation or flutter, vasopressor use, mechanical ventilation, intra-aortic balloon pump or Impella, and pulmonary artery catheter.

multidisciplinary team approach in CS, including involvement of an HF specialist, is associated with improved long-term outcomes, and at the time of discharge, higher rates of initiation of guideline-directed medical therapy.[18,19] Within our own healthcare system, the proposal has been made that making use of existing regional relationships, and infrastructure established for ST-elevation myocardial infarction networks, can provide more timely and equitable access to CS care and improve the survival rate.[20]

In March of 2021, a CS team was established at our institution, along with a standardized CS algorithm. Future studies evaluating the patient populations before and after this time period will be of interest as a means to understand whether these protocols are able to identify potential candidates who may not have been transferred to a specialized centre previously. Further mixed-methods studies also are required to explore barriers at both hospital sites, as is work to build relationships among hospitals, and to allow for early disease recognition, early notification and transfer, and an understanding of the utility of CS teams and algorithms upon a patient's arrival to a CS site.

Limitations

Our study has several limitations. This study was conducted at a single centre and focused on a population of patients with CS who were admitted to the CICU at a centre focused on advanced HF therapies. Thus, the generalizability of our findings to other hospital sites, which may have different expertise, may be limited. We also work in a healthcare system in which referral patterns are based upon level of care and patient needs; given this, the findings may not be generalizable to other healthcare systems. Additionally, given that tracking of all calls relating to cases of CS across the province is not centralized, we were unable to define the true denominator indicating the number of patients who were referred for a potential transfer (but were declined or were not ultimately transferred), or who died prior to transfer or en route to our quaternary-care centre. We also were unable to capture the total length of hospital stay, readmission rates, or number of deaths at outside hospitals, or whether they were seen for follow-up care by a HF specialist or cardiologist once they were transferred back to the sending facility. Lastly, the statistical methods did not account for or test for multiplicity within our study population, because our goal was not to prove, but rather to explore and better understand this CICU population with CS.

Conclusions

In this study of a single, quaternary-care centre, patients transferred from outside hospitals for CS were found to be younger, with fewer comorbidities, and they required more interventions prior to admission and during their CICU admission, including pulmonary artery catheter use, mechanical ventilation, IABP or Impella support, and RRT use. Patients transferred from outside hospitals were less likely to undergo OHT and more likely to require ECLS. Although no differences occurred in in-hospital and 30-day mortality rates from the time of CICU admission, overall, the rates of all-cause mortality at follow-up were lower, and these patients were less likely to meet the composite endpoint of all-cause mortality, ventricular assist device, and OHT, when adjusted for clinically important variables. This study highlights that profiles of patients with CS who are transferred from outside hospitals have inherent differences from those for patients admitted to a specialized CS centre. Future studies evaluating decision-making for CS transfer, as well as the patient populations before and after establishment of a shock team and standardized algorithms, will be of interest to

determine whether potential candidates who were not previously transferred are identified, and whether any differences in outcomes occur.

Ethics Statement

The University Health Network research ethics board review committee approved this study.

Patient Consent

The authors confirm that patient consent is not applicable to this article. As this is a registry, the local research ethics board has provided a waiver of consent (ID#: QIRC 23-0581).

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2024.07.017.