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Original Article

Percutaneous Left Ventricular Assist Device in Cardiogenic Shock: A Five-Year Single Canadian Center Initial Experience

Cvetan Trpkov, MD,[a,‡] Jordan D. Gibson, MD,[b,‡] Robert J.H. Miller, MD,[a] Andrew D.M. Grant, MD,[a] Gregory Schnell, MD,[a] Bryan J. Har, MD, MPH,[a] and Brian Clarke, MD[a]

[a] *Libin Cardiovascular Institute, University of Calgary, Calgary, Alberta, Canada*

[b] *Department of Medicine, University of Calgary, Calgary, Alberta, Canada*

ABSTRACT

Background: Mechanical circulatory support in cardiogenic shock (CS) with percutaneous left ventricular assist devices (PVADs) has expanded rapidly, but there is a paucity of Canadian data. Conflicting observational reports have emerged regarding the benefit of PVADs in CS. We describe a 5-year experience with Impella CP for CS at a single Canadian tertiary care centre.

Methods: Consecutive adult patients with CS supported with Impella CP were included. Comprehensive clinical data and outcomes were retrospectively assessed. We evaluated patient characteristics, patterns of care, in-hospital outcomes, 6-month survival, and predictors of survival.

Results: Thirty-four patients were supported with Impella CP for CS over 5 years. A majority had acute myocardial infarction (94%) with advanced CS (68% Society for Cardiovascular Angiography and

RÉSUMÉ

Contexte : L'assistance circulatoire mécanique en cas de choc cardiogénique (CC) avec des dispositifs d'assistance ventriculaire gauche percutanée s'est rapidement développée, mais les données canadiennes restent rares. Des rapports d'observation contradictoires ont émergé concernant les avantages des dispositifs d'assistance ventriculaire gauche percutanée en cas de CC. Nous décrivons une expérience de cinq ans avec l'Impella CP pour les CC dans un seul centre de soins tertiaires canadien.

Méthodes : Des patients adultes assistés par l'Impella CP, consécutivement à un CC, ont été inclus. Les données et les conclusions cliniques détaillées ont été évaluées rétrospectivement. Nous avons évalué les caractéristiques des patients, les modèles de soins, les bilans en milieu hospitalier, la survie à six mois et les indicateurs de survie.

Despite advances in contemporary therapy, the mortality in acute myocardial infarction with cardiogenic shock (AMICS) remains approximately 50%.[1] The only strategy proven to improve outcomes is early revascularization.[2] The pathophysiology of AMICS is complex—systemic hypoperfusion from low cardiac output causes end-organ dysfunction, hypoxemia, inflammation, and further myocardial ischemia.[3-5] The use of temporary mechanical circulatory support (MCS) to augment cardiac output and mitigate this deleterious cascade is an attractive strategy that may improve outcomes.[6] Clinical trial evidence has failed to demonstrate meaningful improvement in outcomes with the intra-aortic balloon pump (IABP) despite its widespread use in AMICS.[7] The modest effects of IABP on cardiac output may provide insufficient support, highlighting a need for novel strategies.

Temporary percutaneous left ventricular assist devices (PVADs), such as Impella (Abiomed, Inc, Danvers, MA), can augment cardiac output to a much greater extent than IABP and have emerged as a promising tool in AMICS.[8] In contrast to venoarterial extracorporeal membrane oxygenation (VA-ECMO) that increases left ventricular afterload and myocardial wall stress, Impella unloads the left ventricle and increases coronary perfusion pressure.[9-11]

A small randomized trial compared Impella CP with IABP in patients with AMICS and showed no reduction in 30-day mortality.[12] A majority of patients in this study suffered cardiac arrest and the most frequent cause of death was neurological, potentially obviating a benefit of Impella CP support.

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Ethics Statement: This research adheres to relevant ethical guidelines.

‡Co-first authors.

Corresponding author: Dr Brian Clarke, C843, 1403 29 St NW, Calgary, Alberta T2N 2T9, Canada. Tel.: +1-403-944-0120; fax: +1-403-944-3262.

E-mail: brian.clarke@ahs.ca

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Intervention [SCAI] stage D or E). Survival to discharge was 58%. In patients who survived to discharge, 6-month survival was 100% with excellent functional status. SCAI CS stage and initial serum lactate showed significant associations with survival. There was also a trend towards improved survival with shorter door-to-PVAD time. Clinically significant bleeding was common (26%), and 3 patients had device-related vascular complications.

Conclusion: Impella CP may have a role in carefully selected patients with CS. The SCAI shock classification and serum lactate may facilitate patient selection, and minimizing door-to-support time as well as bleeding complications are important considerations. Further clinical investigations, particularly in a Canadian setting, will be necessary to establish the role of this new technology in CS.

Résultats : Trente-quatre patients ont été pris en charge avec l'Impella CP pour un CC sur une période de cinq ans. Une majorité d'entre eux ont subi un infarctus aigu du myocarde (94 %) avec un CC avancé (68 % au stade D ou E sur l'échelle de la Society for Cardiovascular Angiography and Intervention [SCAI]). La survie jusqu'au congé hospitalier était de 58 %. Chez les patients qui ont survécu jusqu'à leur congé de l'hôpital, la survie à six mois était de 100 % avec un excellent état fonctionnel. Le stade de leur CC selon la SCAI et le lactate sérique initial ont montré des associations significatives avec le taux de survie. On a également constaté une tendance à l'amélioration de la survie avec un temps de porte à dispositifs d'assistance ventriculaire gauche percutanée raccourci. Des hémorragies importantes étaient fréquentes (26 %) et trois patients présentaient des complications vasculaires liées au dispositif.

Conclusion : L'Impella CP pourrait avoir un rôle chez des patients atteints de CC soigneusement sélectionnés. La classification du choc selon la SCAI et le niveau de lactate sérique peuvent faciliter la sélection des patients, et la réduction du temps de « porte à assistance » ainsi que les complications hémorragiques constituent des considérations d'importance. D'autres investigations cliniques, en particulier dans un contexte canadien, seront nécessaires pour établir le rôle de cette nouvelle technologie dans le CC.

The Detroit Cardiogenic Shock Initiative investigators developed and implemented a novel AMICS protocol based on PVAD support. The authors report an improved survival rate in AMICS from 51% to 76% after protocol implementation.[13] A similar protocol that emphasized a multidisciplinary cardiogenic shock (CS) team approach also significantly reduced in-hospital mortality compared with historical outcomes at a single centre.[14]

Impella use has expanded dramatically in the United States and Europe; however, there are few published data from a Canadian setting.[15-17] We describe the use of Impella CP for CS at a single Canadian tertiary centre. We report patient characteristics, implant procedure details, complications, and long-term outcomes. We highlight the challenges and opportunities for this therapeutic strategy in a Canadian setting, which presents unique geographical and health system considerations.

Material and Methods

This study is a retrospective cohort of consecutive adult patients (> 18 years old) with CS treated with Impella CP at Foothills Medical Center (FMC) in Calgary, Alberta, Canada. FMC is a 1000+-bed regional cardiovascular referral centre with a catchment area of approximately 2 million people. FMC houses the only cardiac catheterization laboratory and provides all cardiovascular surgery in southern Alberta. There is a dedicated cardiovascular intensive care unit (CICU), and a full spectrum of MCS including temporary and durable surgical ventricular assist devices are offered. Impella CP has been used since June 2014. CS was diagnosed by standard clinical and haemodynamic criteria (Fig. 1).[5]

Comprehensive clinical data were obtained from electronic medical records, paper charts, and the provincial cardiovascular research database (**A**lberta **P**rovincial **Pr**oject for **O**utcome **A**ssessment in **C**oronary **H**eart Disease). Abstracted data included demographic information, past medical history, presentation time to peripheral emergency departments and FMC, emergency room vital signs, emergency room management details (ie, initiation of vasopressors or mechanical ventilation), catheterization procedure details, and complications during hospitalization. We collected admission laboratory data, blood transfusions, vasopressor requirements, ventilation requirements, IABP use and duration, and PVAD support duration. Left ventricular function at admission was assessed by angiography and/or echocardiography. We retrospectively classified each patient according to the recent Society for Cardiovascular Angiography and Interventions (SCAI) CS classification.[18] The vasopressor-inotrope score (VIS) was calculated for each patient at admission and 24 hours for patients still alive.[19] Bleeding was classified by the **G**lobal **U**se of **S**treptokinase and **T**PA for **O**ccluded Arteries (GUSTO) criteria.[20] Device-related vascular complications were defined as major bleeding requiring device explanation, limb ischemia, or vessel injury requiring repair. When calculating symptom to MCS-support time, the estimated onset of ischemic symptoms was defined as time = 0. Six-month survival and cerebral performance category were ascertained through electronic review chart review.

To contextualize CS management at our centre, we also included a representative cohort of all patient admissions to the FMC CICU for calendar year 2015. We used electronic medical record data to identify patients with evidence of CS. CS criteria included sustained systolic blood pressure <90 mm Hg for at least 30 minutes or need for inotropic drugs or MCS, and evidence of end-organ dysfunction. Markers of end-organ dysfunction were elevated lactate (> 2.0 mmol/L) or acute kidney injury defined by the Kidney Disease Improving Global Outcomes criteria (a rise in serum creatinine of $\geq$ 26.5 mmol/L in 48 hours, increase in serum creatine to 1.5 times the known baseline, or reduction in urine output to < 0.5 mL/kg/h for at least 6 hours).[21]

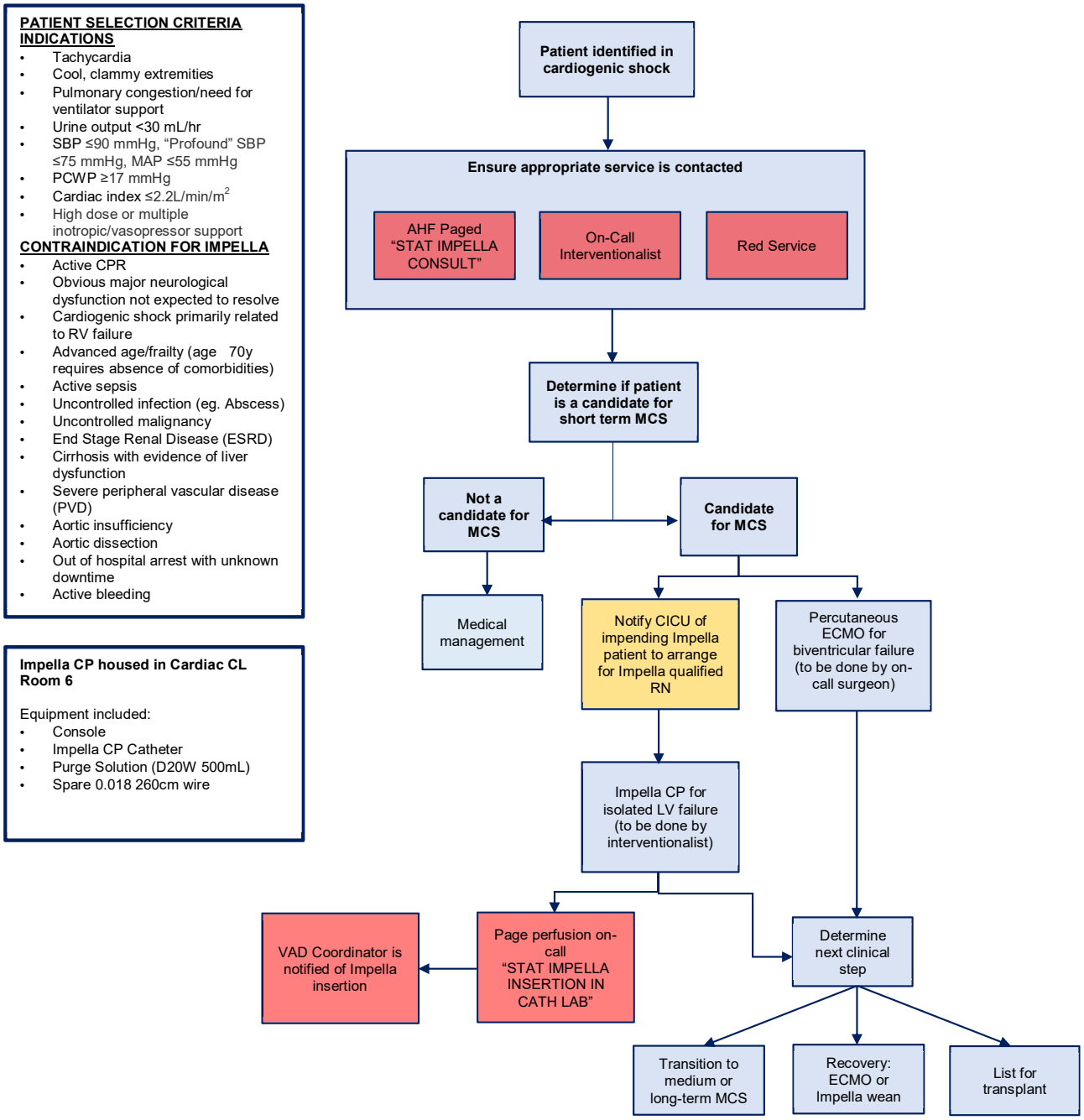

Figure 1. Foothills Medical Centre Impella CP cardiogenic shock protocol. CICU, cardiovascular intensive care unit; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; LV, left ventricular; MCS, mechanical circulatory support; PCWP, pulmonary capillary wedge pressure; RN, registered nurse; RV, right ventricular; SBP, systolic blood pressure; VAD, ventricular assist device.

Data were summarized with descriptive statistics. We compared survivors vs nonsurvivors using Fisher's exact test for discrete variables and Student's *t*-test for continuous variables. Associations with survival to hospital discharge were assessed with univariable logistic regression. Given the limited sample size, multivariable modelling was not performed. All statistical tests were 2-sided, and a P value of < 0.05 was considered significant. Analysis was performed with Microsoft Excel, Wolfram Alpha Prism Graph Pad, and Stata version 13 (StataCorp, College Station, TX). The study was approved by the Institutional Review Board at the University of Calgary.

Results

The MCS protocol and complete patient selection criteria are shown in Figure 1. Patient referrals came from interventional cardiology or CICU. The decision to initiate MCS was made jointly between interventional cardiology, advanced heart failure, cardiac surgery, and the CICU

attending physician. Patients with biventricular failure or severe respiratory failure generally received VA-ECMO and are not included in the present series. During one representative year, there were 1986 admissions to the FMC CICU including 305 patients with evidence of CS by screening criteria. CICU mortality for patients without CS criteria was only 0.5%, whereas patients with CS criteria had CICU mortality of 17%. During this year, 61% of the patients with CS had a primary diagnosis of acute coronary syndrome, 71 patients had an IABP, and 15 underwent Impella CP support.

Impella CP patient characteristics

In total 34 patients with CS were supported with Impella CP over a 5-year period (Fig. 2). Impella CP patient characteristics are provided in Table 1. The mean age of patients was 56.6 years and 29% were female. Vascular risk factors were common (hypertension 44%, diabetes 35%, current smoking 29%), but few patients had a history of prior myocardial infarction or coronary revascularization. A majority of patients had AMICS (94%). Twenty-six patients presented with ST elevation myocardial infarction (76%), 6 with non-ST elevation myocardial infarction (18%), 1 with myocarditis, and 1 with decompensated cardiomyopathy. At initial presentation, 55% of patients were mechanically ventilated, 65% were supported with vasoactive medications, and 24% had out-of-hospital cardiac arrest. Patients with cardiac arrest underwent targeted temperature management to 36°C. Twenty-six patients (76.4%) were transferred from peripheral hospitals and 8 patients (23.5%) presented directly to FMC. Fifteen patients came from peripheral hospitals with a mean transport distance of 186 km.

At arrival, the average mean arterial pressure was 72 mm Hg, pulse was 94 beats/min, and the mean left ventricular end diastolic pressure was 28 mm Hg. The mean Global Registry for Acute Coronary Events score was 167.5, and 23 patients (68%) were SCAI stage D or E. The mean initial serum lactate was 4.3 mmol/L, and peak high sensitivity troponin-T was 16,140 ng/L. Twenty-six patients had severe (left ventricular ejection fraction 21%-30%, 11 patients) or very severe left ventricular systolic dysfunction (left ventricular ejection fraction <20%, 15 patients).

Cardiac catheterization and device implant

Cardiac catheterization and device implant details are provided in Table 2. All Impella CP devices were implanted in the femoral artery. Among the 32 patients with AMICS, culprit arteries were left anterior descending (13), multivessel (8), left main (5), right coronary artery (3), and left circumflex (3). Twenty-seven patients (84%) underwent angioplasty (second-generation drug eluting stents) and 3 underwent coronary artery bypass grafting. Among all patients 50% had initial haemodynamic support with IABP. Eleven patients (32%) required resuscitation from cardiac arrest or unstable ventricular arrhythmia during cardiac catheterization. Impella CP was implanted during the initial cardiac catheterization procedure in 23 patients (68%), before angioplasty in 3 patients (9%), and after clinical deterioration following revascularization and initial support in CICU in 11 patients (32%). There was a trend towards shorter door-to-MCS over

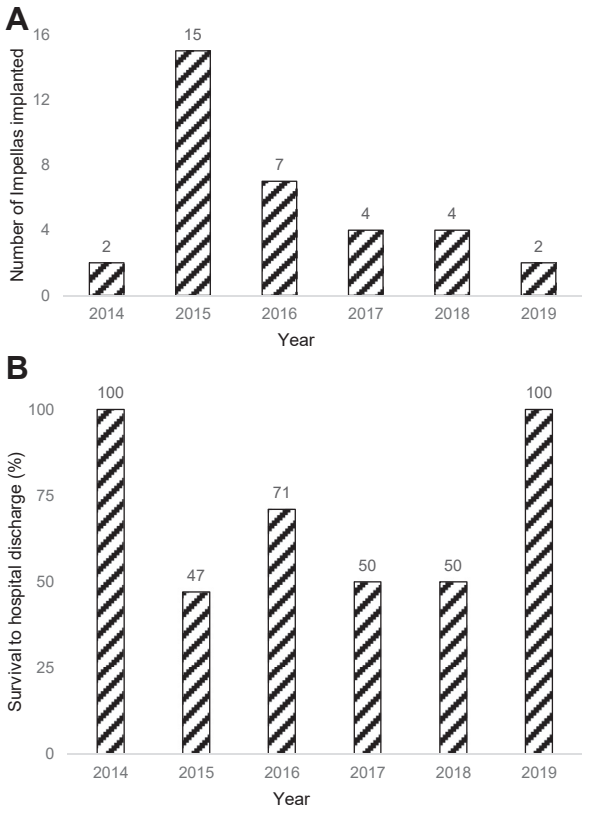

Figure 2. (**A**) Number of percutaneous left ventricular assist devices (PVADs) implanted for cardiogenic shock at Foothills Medical Center (FMC) by year. (**B**) Survival to hospital discharge (%) by year. Note that 2014 and 2019 did not capture full calendar years.

time (Fig. 3). The mean arrival to Impella CP implant time was 16.1 hours until 2016 and 6.7 hours from 2017 onwards ($P = 0.14$). Over the entire study period, 17 patients (50%) had Impella CP implanted within 2 hours of arrival. Survival to discharge amongst patients receiving MCS within and after 2 hours of arrival to FMC was 65% and 53%, respectively ($P = 0.728$).

Outcomes and complications

Outcomes and complications are detailed in Table 3. The mean length of CICU stay was 8 days, and the mean duration of Impella CP support was 58.2 hours. Fifteen patients (44%) had a Swan-Ganz catheter implanted, and the mean initial VIS was 18.6. The mean duration of mechanical ventilation was 79.3 hours, and only 2 patients required renal replacement therapy. Five patients required additional support with VA-ECMO, and Impella CP was implanted for LV venting after VA-ECMO support in 1 patient.

Twenty-one patients (62%) survived to CICU discharge, and 20 patients (59%) survived to hospital discharge; 8 of 14 (57%) nonsurvivors died within 24 hours of Impella CP implantation. Two patients received permanent left ventricular assist devices, and both ultimately underwent successful cardiac transplantation. All discharge survivors were alive at 6 months, and the mean cerebral performance category among these patients was 1.05.

Table 1. Percutaneous left ventricular assist device cardiogenic shock patient characteristics

	Total (N = 34)	Survivors (N = 20)	Nonsurvivors (N = 14)	*P* value
Demographics				
Age (±SD)	56.6 (12.5)	56.7 (14.7)	56.5 (9.1)	0.971
Female	10 (29.4%)	5 (25.0%)	5 (35.7%)	0.704
BMI (±SD)	29.2 (6.6)	28.8 (6.6)	29.7 (6.9)	0.734
Current smoking	10 (29.4%)	7 (35.0%)	3 (21.4%)	0.467
Hypertension	15 (44.1%)	6 (30.0%)	9 (65.3%)	0.080
Diabetes mellitus	12 (35.3%)	5 (25.0%)	7 (50.0%)	0.163
Prior CAD	4 (11.8%)	2 (10.0%)	2 (14.3%)	1.000
Prior stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
Prior PCI/CABG	2 (5.9%)	1 (5.0%)	1 (7.1%)	1.000
Cardiac arrests	12 (35.3%)	7 (35.0%)	5 (35.7%)	1.000
OHCA	8 (23.5%)	5 (25.0%)	3 (21.4%)	1.000
Etiology				
STEMI	26 (76.5%)	17 (85.0%)	9 (64.3%)	0.228
NSTEMI	6 (17.6%)	2 (10.0%)	4 (29.6%)	0.202
Other	2 (5.9%)	1 (5.0%)	1 (7.1%)	1.000
Mean GCS (±SD)	12.4 (4.9)	12.4 (4.5)	12.4 (5.1)	0.995
Mechanical ventilation	19 (55.9%)	10 (50.0%)	9 (64.3%)	0.495
Initial vasoactive drugs	21 (61.8%)	11 (55.0%)	10 (71.4%)	0.477
GRACE score (±SD)	167.5 (40.3)	168.0 (28.0)	169.4 (34.4)	0.986
Initial heart rate (bpm) (±SD)	93.7 (24.1)	86.2 (21.2)	105.3 (24.5)	0.030
Initial MAP (mm Hg) (±SD)	72 (15)	73 (15)	70 (14)	0.534
LVEDP (mm Hg) (±SD)	28 (9)	26 (8)	30 (11)	0.323
Initial biochemistry				
Haemoglobin (g/L) (±SD)	143.9 (20.6)	142.8 (19.6)	145.5 (19.6)	0.708
Creatinine (μmol/L) (±SD)	109.7 (43.9)	96.5 (30.0)	128.6 (54.9)	0.060
Lactate (mmol/L) (±SD)	4.3 (3.2)	3.36 (2.9)	5.7 (3.3)	0.049
Troponin (ng/L) (±SD)	6439.7 (9334.4)	7850.5 (11211.0)	4486.15 (5714.4)	0.285
pH (±SD)	7.24 (0.2)	7.29 (0.1)	7.16 (0.2)	0.023
Initial bilirubin (μmol/L) (±SD)	14.1 (4.3)	16.0 (3.5)	11.6 (5.1)	0.305
Initial ALT (IU/L) (±SD)	346.2 (989.6)	153.0 (174.6)	613.6 (1507.2)	0.206
Initial INR (±SD)	1.2 (0.3)	1.2 (0.2)	1.3 (0.5)	0.538
Initial LVEF (%) (±SD)	27.9 (8.9)	24.5 (7.7)	26.5 (8.4)	0.249

Data are presented as n (%) unless specified otherwise.

ALT, alanine transferase; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; GCS, Glasgow coma scale; GRACE, Global Registry of Acute Coronary Events; INR, International Normalized Ratio; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; NSTEMI, non-ST-segment elevation myocardial infarction; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous intervention; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.

Impella CP was explanted because of complications in 2 patients; one device was explanted after entanglement in the mitral valve apparatus and the second after hemorrhage at the femoral artery implantation site. GUSTO moderate/major bleeding occurred in 11 patients (32%). Twenty-two patients (65%) underwent transfusion with an average of 7.6 units of packed red blood cells (median, 1 unit). The most frequent site of major bleeding was the femoral implantation site

Table 2. Cardiac catheterization and device implant

	Total (N = 34)	Survivors (N = 20)	Nonsurvivors (N = 14)	*P* value
Culprit artery				
LAD	13 (38.2%)	7 (35.0%)	6 (42.9%)	0.728
LCx	3 (8.8%)	2 (10.0%)	1 (7.1%)	1.000
RCx	3 (8.8%)	3 (15.0%)	0 (0.0%)	0.251
LM	5 (14.7%)	4 (20.0%)	1 (7.1%)	0.379
MVD	7 (20.6%)	3 (15.0%)	4 (28.6%)	0.410
Graft	1 (2.9%)	0 (0.0%)	1 (7.1%)	0.412
Hospital transfer	26 (76.5%)	13 (65.0%)	13 (92.9%)	0.102
Door to balloon time (min) (±SD)	58.3 (52.8)	48.6 (40.7)	75.3 (69.1)	0.344
PCI performed	27 (79.4%)	16 (80.0%)	11 (78.6%)	1.000
Initial IABP	15 (44.1%)	9 (45.0%)	6 (42.9%)	1.000
Impella at the time of first catheterization	23 (67.6%)	13 (65.0%)	10 (71.4%)	1.000
Impella before PCI	3 (8.8%)	1 (5.0%)	2 (14.3%)	0.556
Symptom to Impella time (h) (±SD)	40.3 (62.9)	38.2 (40.7)	43.3 (69.1)	0.824
Foothills to Impella time (h) (±SD)	13.5 (22.9)	10.3 (14.1)	18.2 (31.7)	0.385
VIS at the time of Impella (±SD)	18.6 (23.7)	11.2 (17.4)	31.5 (28.2)	0.048

Data are presented as n (%) unless specified otherwise.

IABP, intra-aortic balloon pump; LAD, left-anterior descending; LCx, left circumflex; LM, left main; MVD, multivessel disease; PCI, percutaneous intervention; RCx, right coronary; SD, standard deviation; VIS, vasoactive-inotropic score.

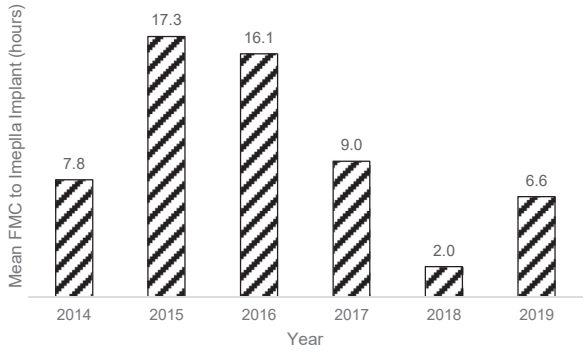

Figure 3. Foothills Medical Center (FMC) to Impella implant time (hours) in patients presenting with cardiogenic shock by year. Note that 2014 and 2019 do not represent full calendar years.

(21%), and other significant bleeding sites included thoracic (9%) and intraperitoneal (6%). Significant vascular complications occurred in 3 cases. One patient with peripheral arterial disease developed worsening limb ischemia and ultimately required below knee amputation. A second patient developed a pseudoaneurysm that was treated successfully with thrombin injection. The third patient developed a massive hemorrhage at the femoral access-site that required repair.

Predictors of survival

The initial serum lactate was lower in survivors vs nonsurvivors (3.36 vs 5.71 mmol/L, $P = 0.049$). Survival was significantly greater among SCAI stage C vs SCAI stage D or E patients (93% vs 43%, $P = 0.011$). Survival among SCAI stage D patients was 53%, whereas no SCAI stage E patients survived (Fig. 4). There was a trend towards higher survival to hospital discharge among patients who presented directly to FMC compared with patients who were transferred (87.5% vs 50.0%, $P = 0.10$). The interval between symptom onset and PVAD implantation was 22.5 hours for directly admitted patients vs 48.5 hours for transferred patients ($P = 0.16$). Unadjusted associations with in-hospital mortality are shown in Table 4. Lower initial serum pH (unadjusted odds ratio [OR], 0.52; $P = 0.025$) and higher VIS score (unadjusted OR, 1.55 per 10 points; $P = 0.043$) were associated with increased in-hospital mortality. Presenting in SCAI stage D/E shock was also associated with in-hospital mortality (unadjusted OR, 13.0; $P = 0.026$).

Discussion

We provide the first detailed report describing the use of Impella CP for CS at a Canadian tertiary care centre. CS accounted for up to 15.4% of admissions to our CICU during 1 representative year. Impella CP support was reserved for the highest acuity cases, and advanced CS (SCAI stage D/E) was present in the majority of patients. Despite this, a significant proportion of these patients survived to discharge and had excellent functional outcomes at 6 months.

A greater proportion of our Impella CP patients had underlying AMI compared with our overall CICU CS population (94% vs 61%). Reasons for this discrepancy may include selection bias, chance effects due to small sample size, and differential prevalence of Impella CP exclusion criteria among patients with non-AMI CS. In addition, Impella CP was reserved for patients with isolated left ventricular failure. In a recent multicentre study from Italy, AMICS was the indication for Impella in 75.1% of cases.[22]

Our data suggest that the SCAI classification combined with initial serum lactate may facilitate identification of candidates for Impella CP support. Optimal patient selection and timing are key factors determining success of MCS. Profound CS may render MCS potentially futile, whereas patients with early-stage CS may improve with medical therapy alone. Determining MCS candidacy and the appropriate MCS modality is a complex, time-limited decision that involves multiple clinicians and often relies on incomplete data. The SCAI classification is straightforward and can be calculated with limited data available at the time of initial patient presentation. This classification scheme predicts survival in CS and has gained rapid acceptance.[23] The SCAI classification could help streamline shock team communication and facilitate MCS selection. In our series, patients with SCAI stage E shock or

Table 3. Outcomes and complications

Clinical management pattern	Total (N = 34)	Survivors (N = 20)	Nonsurvivors (N = 14)	*P* value
Mean VIS at 24 h (±SD)	13.4 (18.0)	10.13 (11.8)	25.9 (31.4)	0.329
Mean delta VIS at 24 h (±SD)	0.9 (17.2)	−1.1 (16.8)	8.3 (18.7)	0.350
Mean length of mechanical ventilation (h) (±SD)	79.3 (111.8)	86.9 (116.5)	68.1 (108.2)	0.643
Complication requiring explant	4 (11.8%)	2 (10.0%)	2 (14.2%)	1.000
CABG during admission	3 (9.1%)	3 (15.0%)	0 (0%)	0.251
GUSTO moderate/major bleeding	11 (26.4%)	6 (25.0%)	5 (28.6%)	1.000
Bleed by location				
Groin	6 (17.6%)	2 (10.0%)	4 (28.7%)	0.202
Retroperitoneal	2 (5.9%)	0 (0.0%)	2 (14.3%)	0.162
Intrathoracic	3 (8.8%)	3 (15.0%)	0 (0.0%)	0.251
Intraperitoneal	2 (5.9%)	2 (10.0%)	0 (0.0%)	0.501
Haemolysis	3 (8.8%)	2 (10.0%)	1 (7.1%)	1.000
Vascular complication	3 (8.8%)	2 (10.0%)	1 (7.1%)	1.000
Stent thrombosis	1 (2.9%)	1 (5.0%)	0 (0.0%)	1.000

Data are presented as n (%) unless specified otherwise.

CABG, coronary artery bypass graft; GUSTO, Global Use of Streptokinase and TPA for Occluded Arteries; SD, standard deviation; VIS, vasoactive-inotropic score.

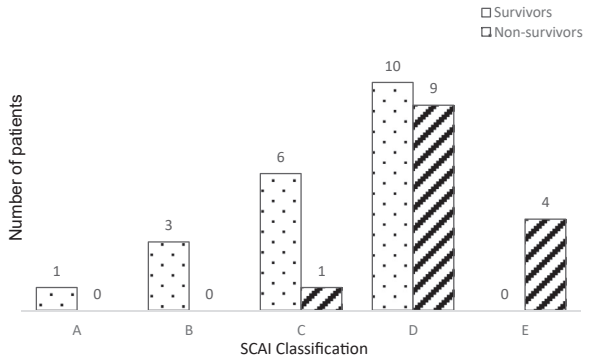

Figure 4. Patient numbers and hospital mortality by Society for Cardiovascular Angiography and Intervention (SCAI) classification.

initial lactate >5 mmol/L had poor outcomes despite Impella CP implantation. Notably, zero patients classified as SCAI stage E survived, and exclusion of these cases yields a survival rate of 67%. It is unclear whether VA-ECMO, which can provide full haemodynamic support, represents a viable MCS strategy among such patients.[24] SCAI stage C or D patients may benefit from Impella CP, with implementation of best practices to further improve outcomes in this group. Patients classified as SCAI A or B may benefit from a trial of medical therapy rather than early MCS.

Survival to hospital discharge among our cohort was comparable with survival in contemporary studies of Impella-supported patients with CS in different parts of the world.[22,25] Improved outcomes have been reported by several institutions after implementation of PVAD CS protocols.[14,24] These protocols, informed by observational data, emphasize 3 key strategies: (1) minimizing time to MCS, (2) active weaning of vasoactive medications, and (3) use of routine invasive haemodynamic measurements to guide therapy. In particular, minimizing the door-to-MCS time has emerged as a potential strategy to improve outcomes in AMICS. For example, Basir et al. reported progressively lower survival when MCS was delayed; patients with MCS within 1.5 hours had 66% survival compared with 26% survival when MCS was delayed to 4.25 hours. The Detroit Cardiogenic Shock Initiative achieved the door-to-MCS time of 1.38 hours and survival to hospital discharge of 75%.[13] In the ongoing National Cardiogenic Shock Initiative, a door-to-MCS target of 90 minutes or less has been established as a treatment target.[24] In our experience, Impella CP support was often reserved as a bail-out therapy and delayed MCS was common with the mean door-to-support of 12.8 hours. A majority of patients in our cohort were treated before the advent of the recent CS protocols, and these strategies were not routinely implemented at our centre. A significant factor in the delay to Impella CP in our cohort was initial support with IABP (44%) or initial medical therapy (9%). In addition, patient transport contributed to delayed MCS, as 11 patients came from communities over 190 km away. Notably, we observed a trend towards shorter door-to-support over time, potentially reflecting the influence of the recent CS protocols on local practice.

It is important to note that CS protocols advocating early, routine MCS have not yet been evaluated through randomized controlled trials. Wider MCS deployment in CS could lead to apparent improved outcomes due to treatment of patients with lower disease severity. For example, patients in our CICU who met CS screening criteria had mortality of only 17%. The outcomes reported in recent observational studies may be subject to confounding, and a randomized trial evaluating early MCS in CS is ongoing.[26]

Several other important observations deserve particular attention. Active weaning of vasoactive drugs was not stipulated at our centre, but we noted a trend towards a reduction in vasoactive drugs among survivors vs escalating doses among nonsurvivors. Vasoactive medications may be harmful in CS, and observational data suggest improved outcomes with fewer vasoactive agents in patients with CS.[25,27] Pulmonary artery catheters were implanted in fewer than half of patients in our cohort (44%). Invasive haemodynamic monitoring in patients with CS who receive MCS may be associated with improved outcomes.[16]

Significant vascular access site bleeding was the most frequent adverse event in our cohort. Recently, observational data suggested a signal of possible harm comparing Impella with IABP and an associated signal of increased bleeding as a possible mechanism.[28-30] This may be related to the large bore vascular access (14 French vs 8 French for IABP), and

Table 4. Univariate regression predictors of in-hospital mortality among Impella CP cardiogenic shock patients

Variable	Unadjusted OR (range)	*P* value
Age (per 10 y)	0.99 (0.57-1.72)	0.972
Male	0.60 (0.14-2.66)	0.502
BMI	1.02 (0.91-1.15)	0.722
Current smoking	1.63 (0.41-6.46)	0.487
Hypertension	4.20 (0.98-17.9)	0.053
Diabetes mellitus	3.00 (0.70-12.9)	0.139
Prior CAD	1.50 (0.19-12.1)	0.704
Prior PCI/CABG	1.46 (0.08-25.5)	0.795
Cardiac arrest	1.03 (0.25-4.30)	0.966
STEMI	0.32 (0.06-1.64)	0.171
GCS	0.99 (0.86-1.14)	0.932
Mechanical ventilation	1.80 (0.44-7.31)	0.411
Initial HR	1.00 (0.98-1.03)	0.703
Initial MAP	0.97 (0.94-1.01)	0.121
LVEDP	1.04 (0.96-1.12)	0.364
Haemoglobin (g/L)	1.01 (0.97-1.04)	0.704
Creatinine (μmol/L)	1.02 (1.00-1.04)	0.053
Lactate (mmol/L)	1.29 (0.99-1.67)	0.058
Troponin (ng/L)	1.00 (1.00-1.00)	0.302
pH (per 0.1)	0.52 (0.30-0.92)	0.025
Initial bilirubin	0.95 (0.86-1.05)	0.328
Initial ALT	1.00 (1.00-1.00)	0.443
Initial INR	1.94 (0.25-15.2)	0.530
Initial LVEF < 20%	2.48 (0.61-10.1)	0.205
Initial vasoactive drugs (per 10 points)	1.55 (1.01-2.36)	0.043
GRACE score (per 10 points)	1.00 (0.84-1.19)	0.986
Door to balloon time (per 10 min)	1.00 (0.99-1.01)	0.969
PCI performed	0.92 (0.17-4.93)	0.919
Symptom to Impella time (per h)	1.01 (0.99-1.02)	0.476
SCAI stage D/E vs A/B/C	13.0 (1.4-119.0)	0.023

ALT, alanine transferase; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; GCS, Glasgow coma scale; GRACE, Global Registry for Acute Coronary Events; HR, heart rate; INR, International Normalized Ratio; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; OR, odds ratio; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Intervention; STEMI, ST-segment elevation myocardial infarction.

adoption of routine ultrasound guidance may reduce access complications.[31,32] An Impella arteriotomy preclosure technique has also been described.[33] In addition, these patients were critically ill with multiple metabolic derangements, including hepatic dysfunction, which can contribute to coagulopathy. Moreover, patients frequently had chest trauma from cardiopulmonary resuscitation, were exposed to multiple antithrombotic agents, and may develop acquired Von Willebrand syndrome due to high blood shear forces caused by Impella CP.[33,34] Reducing bleeding complications represents a major goal towards achieving successful outcomes.

This study is limited by its retrospective design and small numbers, but the trends observed are still informative. Although all PVADs were implanted in accordance with a local protocol, the device implantation was inherently subject to treatment bias, which may have overestimated the treatment effect. We did not include a matched comparison group, such as patients with AMICS supported with IABP. Finding appropriate matched IABP controls for our cohort would be difficult because PVAD support was reserved for higher acuity patients at our institution and selection bias would be significant. In addition, a small sample size precluded multivariate statistical analysis.

Conclusion

In summary, we report real-world initial experiences of MCS with Impella CP for CS at a single Canadian tertiary care centre. Our results illustrate the ongoing need for more discreet patient selection criteria and suggest that this may be achieved through incorporation of the novel SCAI CS classification and serum lactate measurement. Minimizing door-to-MCS time in these appropriately selected patients, reducing bleeding, and avoiding implant in advanced stages of CS are important variables to consider. Ongoing clinical evaluation is needed as there are conflicting signals from observational studies on adequately powered clinical trials of PVADs such as Impella CP in CS. Canadian centres considering a PVAD program may benefit from the development of a Canadian randomized controlled trial or an observational study with multicentre harmonized protocols.

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References

1. Thiele H, Akin I, Sandri M, et al. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. N Engl J Med 2017;377:2419-32.
2. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. N Engl J Med 1999;341:625-34.
3. Cooper HA, Panza JA. Cardiogenic shock. Cardiol Clin 2013;31:567-80.
4. Thiele H, Allam B, Chatellier G, Schuler G, Lafont A. Shock in acute myocardial infarction: the Cape Horn for trials? Eur Heart J 2010;31:1828-35.
5. van Diepen Sean, Katz Jason N, Albert Nancy M, et al. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. Circulation 2017;136:e232-68.
6. Hajjar LA, Teboul J-L. Mechanical circulatory support devices for cardiogenic shock: state of the art. Crit Care 2019;23:76.
7. Thiele H, Zeymer U, Neumann F-J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med 2012;367:1287-96.
8. Seyfarth M, Sibbing D, Bauer I, et al. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol 2008;52:1584-8.
9. Kawashima D, Gojo S, Nishimura T, et al. Left ventricular mechanical support with Impella provides more ventricular unloading in heart failure than extracorporeal membrane oxygenation. ASAIO J 2011;57:169-76.
10. Sauren LDC, Accord RE, Hamzeh K, et al. Combined Impella and intra-aortic balloon pump support to improve both ventricular unloading and coronary blood flow for myocardial recovery: an experimental study. Artif Organs 2007;31:839-42.
11. Saku K, Kakino T, Arimura T, et al. Left ventricular mechanical unloading by total support of Impella in myocardial infarction reduces infarct size, preserves left ventricular function, and prevents subsequent heart failure in dogs. Circ Heart Fail 2018;11:e004397.
12. Ouweneel DM, Eriksen E, Sjauw KD, et al. Percutaneous mechanical circulatory support versus intra-aortic balloon pump in cardiogenic shock after acute myocardial infarction. J Am Coll Cardiol 2017;69:278-87.
13. Basir MB, Schreiber T, Dixon S, et al. Feasibility of early mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: The Detroit Cardiogenic Shock Initiative. Catheter Cardiovasc Interv 2018;91:454-61.
14. Tehrani BN, Truesdell AG, Sherwood MW, et al. Standardized team-based care for cardiogenic shock. J Am Coll Cardiol 2019;73:1659-69.
15. Burzotta F, Trani C, Doshi SN, et al. Impella ventricular support in clinical practice: collaborative viewpoint from a European expert user group. Int J Cardiol 2015;201:684-91.
16. O'Neill WW, Grines C, Schreiber T, et al. Analysis of outcomes for 15,259 US patients with acute myocardial infarction cardiogenic shock (AMICS) supported with the Impella device. Am Heart J 2018;202:33-8.
17. Gauthier S, Sharma D, Abdel-Hadi H, et al. Predictors of 30-day mortality and outcomes in patients who receive percutaneous left-ventricular support with an Impella assist device. Can J Cardiol 2015;31:S24-5.
18. Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: this document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. Catheter Cardiovasc Interv 2019;94:29-37.

19. Na SJ, Chung CR, Cho YH, et al. Vasoactive inotropic score as a predictor of mortality in adult patients with cardiogenic shock: medical therapy versus ECMO. Rev Esp Cardiol (Engl Ed) 2019;72:40-7.

20. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research consortium. Circulation 2011;123:2736-47.

21. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012;120:c179-84.

22. Chieffo A, Ancona MB, Burzotta F, et al. Observational multicentre registry of patients treated with IMPella mechanical circulatory support device in ITaly: the IMP-IT registry. EuroIntervention 2020;15:e1343-50.

23. Jentzer JC, van Diepen S, Barsness GW, et al. Cardiogenic shock classification to predict mortality in the cardiac intensive care unit. J Am Coll Cardiol 2019;74:2117-28.

24. Basir MB, Kapur NK, Patel K, et al. Improved outcomes associated with the use of shock protocols: updates from the National Cardiogenic Shock Initiative. Catheter Cardiovasc Interv 2019;93:1173-83.

25. Basir MB, Schreiber TL, Grines CL, et al. Effect of early initiation of mechanical circulatory support on survival in cardiogenic shock. Am J Cardiol 2017;119:845-51.

26. Udesen NJ, Møller JE, Lindholm MG, et al. Rationale and design of DanGer shock: Danish-German cardiogenic shock trial. Am Heart J 2019;214:60-8.

27. Adams KF, Fonarow GC, Emerman CL, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J 2005;149:209-16.

28. Schrage Benedikt, Ibrahim Karim, Loehn Tobias, et al. Impella support for acute myocardial infarction complicated by cardiogenic shock. Circulation 2019;139:1249-58.

29. Dhruva SS, Ross JS, Mortazavi BJ, et al. Association of use of an intravascular microaxial left ventricular assist device vs intra-aortic balloon pump with in-hospital mortality and major bleeding among patients with acute myocardial infarction complicated by cardiogenic shock. JAMA 2020;323:734-45.

30. Amin AP, Spertus JA, Curtis JP, et al. The evolving landscape of Impella use in the United States among patients undergoing percutaneous coronary intervention with mechanical circulatory support. Circulation 2020;141:273-84.

31. Seto AH, Abu-Fadel MS, Sparling JM, et al. Real-time ultrasound guidance facilitates femoral arterial access and reduces vascular complications: FAUST (Femoral Arterial Access with Ultrasound Trial). JACC Cardiovasc Interv 2010;3:751-8.

32. Kaki A, Blank N, Alraies MC, et al. Access and closure management of large bore femoral arterial access. J Interv Cardiol 2018;31:969-77.

33. Lata K, Kaki A, Grines C, et al. Pre-close technique of percutaneous closure for delayed hemostasis of large-bore femoral sheaths. J Interv Cardiol 2018;31:504-10.

34. Davis ME, Haglund NA, Tricarico NM, Keebler ME, Maltais S. Development of acquired von Willebrand syndrome during short-term micro axial pump support: implications for bleeding in a patient bridged to a long-term continuous-flow left ventricular assist device. ASAIO J 2014;60:355-7.