Long-term mortality and costs following use of Impella® for mechanical circulatory support: a population-based cohort study

Mortalité à long terme et coûts liés à l'utilisation de l'Impella® pour une assistance circulatoire mécanique: une étude de cohorte populationnelle

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Abstract

Purpose The Impella® device is a form of mechanical circulatory support (MCS) used in critically ill adults with cardiogenic shock. We sought to evaluate short- and long-term outcomes following the use of Impella, including mortality, healthcare utilization, and costs.

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Methods Population-based, retrospective cohort study of adult patients (≥ 16 yr) receiving Impella in Ontario, Canada (1 April 2012–31 March 2019). We captured outcomes through linkage to health administrative databases. The primary outcome was mortality during hospitalization. Secondary outcomes included mortality at 30 days, 90 days, and one year following Impella insertion. We analyzed health system costs in Canadian dollars in the year following the date of the index admission, including the costs of inpatient admission.

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Results We included 162 patients. Mean (standard deviation) age was 59.2 (14.5) yr, and 73.5% of patients were male. Median [interquartile range (IQR)] time to Impella insertion from date of hospital admission was 2 [1–9] days. In-hospital mortality was 56.8%, and a significant proportion of patients were bridged to a ventricular assist device (67.9%). Mortality at one year was 61.7%. Among hospital survivors, only 38.6% were discharged home independently. Median [IQR] total cost in the year following admission among all patients was \$88,397 [32,718–225,628], of which \$66,529 [22,789–183,165] was attributed to inpatient care.

Conclusions In-hospital mortality among patients with cardiogenic shock receiving Impella is high, but with minimal increase at one year. While Impella patients accrued substantial costs, these largely reflected inpatient costs, and not costs incurred following hospital discharge.

Résumé

Objectif Le dispositif Impella® est un système d'assistance circulatoire mécanique utilisé chez les adultes en état critique souffrant d'un choc cardiogénique. Nous avons souhaité évaluer les issues à court et à long terme liées à l'utilisation de l'Impella, notamment la mortalité, l'utilisation des soins de santé et les coûts.

Méthode Nous avons réalisé une étude de cohorte rétrospective basée sur une population de patients

adultes (≥ 16 ans) recevant un Impella en Ontario, au Canada (1^{er} avril 2012–31 mars 2019). Nous avons saisi les données pertinentes à nos critères d'évaluation en créant des liens avec les bases de données administratives de santé. Le critère d'évaluation principal était la mortalité pendant l'hospitalisation. Les critères d'évaluation secondaires comportaient la mortalité à 30 jours, 90 jours et un an après l'insertion de l'Impella. Nous avons analysé les coûts pour le système de santé en dollars canadiens au cours de l'année suivant la date d'admission initiale, notamment les coûts hospitaliers.

Résultats Nous avons inclus 162 patients. L'âge moyen (écart type) était de 59,2 (14,5) ans, et 73,5 % des patients étaient des hommes. Le temps médian [écart interquartile (ÉIQ)] jusqu'à insertion de l'Impella depuis l'admission à l'hôpital était de 2 [1–9] jours. La mortalité hospitalière était de 56,8 %, et un dispositif d'assistance ventriculaire a été implanté chez une importante proportion de patients (67,9 %). La mortalité à un an était de 61,7 %. Parmi les survivants hospitaliers, seuls 38,6 % ont reçu leur congé pour un retour indépendant à la maison. Le coût total médian [ÉIQ] pour l'année suivant l'admission parmi tous les patients était de 88 397 \$ [32 718 – 225 628 \$], dont 66 259 \$ [22 789 – 183 165 \$] étaient attribuables aux soins hospitaliers.

Conclusion La mortalité hospitalière parmi les patients en choc cardiogénique chez lesquels un Impella est installé est élevée, mais on n'observe qu'une augmentation minimale à

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un an. Alors que les patients ayant reçu un Impella ont engendré des coûts importants, ces coûts reflètent principalement les coûts hospitaliers et non les coûts encourus après le congé de l'hôpital.

Keywords Impella · cardiogenic shock · mechanical circulatory support · health services

Cardiogenic shock is a clinical condition characterized by systemic global hypoperfusion secondary to cardiac dysfunction. Mortality from this condition has been estimated to be between 50 and 80%, depending on the clinical context.^{1,2} While cardiogenic shock is typically managed with vasoactive medications, inotropes, and attempts to reverse underlying pathology (e.g., through revascularization), clinicians are increasingly turning to mechanical circulatory support (MCS) to manage this high-risk population.³ Among the MCS devices used for the care of patients with cardiogenic shock is the intravascular microaxial blood pump called Impella® (Abiomed Inc., Danvers, MA, USA).⁴ Impella devices are catheter-based and function as a miniaturized ventricular assist pump. Impella devices therefore increase cardiac output, and have additional benefits of reducing left ventricular (LV) afterload, LV end-diastolic pressure, and myocardial oxygen consumption.⁵ For these reasons, they have become an attractive option for MCS in patients with cardiogenic shock, and are primarily used in Ontario for this indication.⁶

Despite the potential physiologic benefits of Impella devices, existing evidence does not support improved efficacy of Impella in the acute management of cardiogenic shock compared with other MCS devices, such as intra-aortic balloon pumps (IABP), or veno-arterial extracorporeal membrane oxygenation (ECMO). Observational studies have provided heterogeneous results, with some suggesting that Impella use is associated with higher survival rates in patients with cardiogenic shock,^{7–9} while others have found Impella to be associated with higher rates of hospital mortality and adverse events compared with IABP.^{10–12} The only large-scale randomized trial conducted in this area (PROTECT II) found Impella was not superior to IABP in reducing short-term major adverse cardiac events¹³; but this trial was limited to patients receiving high-risk percutaneous coronary intervention (PCI), and did not exclusively include those with cardiogenic shock. Despite a lack of evidence showing benefit, the use of this invasive and expensive technology has grown significantly in the United States, though variably across centres.¹⁰

Multicentre data on long-term outcomes following the use of Impella are lacking. Furthermore, little is known regarding short- and long-term patient-level costs associated with Impella, particularly outside of acute-care sectors. Cost-effectiveness has become an important consideration in the evaluation of critical care interventions.¹⁴ To investigate these questions, we conducted a population-based cohort study to evaluate the short- and long-term health outcomes and costs of adult patients receiving Impella as MCS. We hypothesized that Impella use would significantly change long-term mortality and cost.

Methods

The ICES studies fall under section 45 of the Personal Health Information Protection Act of Ontario, and as such, do not require research ethics board approval.

Data sources and setting

We conducted a population-based, retrospective cohort study using health administrative databases in Ontario, Canada (population 13 million). In Ontario's predominantly single-payer healthcare system, healthcare databases record all medically necessary healthcare services (including Impella use), as well as physician, hospital, and demographic information of residents. These data are held and linked at ICES, an independent, non-profit custodian of provincial health data. ICES is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. The Impella device is provided at seven tertiary care centres in Ontario: Hamilton Health Sciences Centre (Hamilton, ON, Canada), Health Sciences North (Sudbury, ON, Canada), London Health Sciences Centre (London, ON, Canada), St. Michael's Hospital (Toronto, ON, Canada), University Health Network (Toronto, ON, Canada), University of Ottawa Heart Institute (Ottawa, ON, Canada), and Windsor Regional Hospital (Windsor, ON, Canada).⁶

The following databases are linked then anonymized at the individual level at ICES: 1) The Ontario Health Insurance Plan Claims Database, to capture data on physician fee-for-service claims for inpatient and outpatient services; 2) The Canadian Institute for Health Information Discharge Abstract Database, to capture information on all acute care hospitalizations, including detailed diagnostic and procedural information; 3) The Registered Persons Database, for capturing deaths and all demographic information; 4) The Home Care Database, to capture public-funded homecare services; 5) The National Ambulatory Care Reporting System, to capture information

on emergency department use; 6) The National Rehabilitation Reporting System for inpatient rehabilitation programs; 7) The Continuing Care Reporting System, for data on long-term care (i.e., nursing home) and complex continuing care use; 8) Statistics Canada Census data, for income quintile and rurality through postal codes; and 9) The Ontario Drug Benefit Claims database, for tracking data on prescription medications dispensed among patients at least 65 yr of age eligible for coverage.

Patients

We included adult patients (≥ 16 yr of age) receiving Impella in Ontario from April 1 2012 through March 31 2019. We identified patients whose hospitalization records indicated the presence of an inpatient Impella intervention code by searching through the Discharge Abstract Database (eTable 1, available as Electronic Supplemental Material [ESM]). This includes patients receiving Impella CP, Impella 2.5, or Impella 5.0, although Impella 2.5 is not commonly used in Ontario.⁶ To further validate our patients, we ensured that all included patients had been admitted to a medical, surgical, or cardiac intensive care unit during the index hospitalization.

For each patient, we identified relevant comorbidities using hospitalization data up to two years prior to the date of admission. We further identified the presence of complex chronic diseases among our cohort, using previously described methods (eTable 2 available as ESM).^{15–17} All other conditions were based on the presence of any one inpatient hospital diagnostic code, or two or more outpatient physician billing codes within a two-year period, using relevant International Classification of Diseases (ICD) Version 9 (ICD-9) and ICD-10 codes. Comorbidities identified included history of arrhythmia, history of malignancy, congestive heart failure (CHF), chronic obstructive pulmonary disease, coronary artery disease (CAD), dementia, diabetes mellitus, hypertension, chronic kidney disease, and cerebrovascular disease.

Outcomes

The primary outcome was hospital mortality. Secondary outcomes included mortality at 30 days, 90 days, and one year following Impella insertion. We calculated time to Impella insertion by calculating the difference between the hospital admission date and the date associated with the Impella intervention code. Length of hospital stay was reported from the date of hospital admission to the date of discharge or in-hospital death. We determined discharge disposition using a hierarchy approach (eTable 3 available as ESM). The ICES databases do not contain indices

related to severity of illness (including the IABP-SHOCK II¹⁸ and CardShock Scores,¹⁹ which are specific to cardiogenic shock). We also evaluated “home time” following discharge, which is defined as the number of nights in a private residence. “Home time” has been shown to correlate with common functional scales (such as the modified Rankin Scale).²⁰ As a surrogate for illness severity, we identified other interventions performed during the index admission, including PCI, renal replacement therapy (RRT), ventricular assist device (VAD) implantation, ECMO cannulation, and cardiac transplantation, using the relevant procedural codes in the Discharge Abstract Database.

For patients with available costing data (April 1 2012–March 31 2018), we examined the total and sector-specific direct healthcare costs accumulated in the year following the date of the index hospital admission (including the admission itself). We obtained all records of healthcare use paid for by the Ontario Ministry of Health and Long-term Care following hospital admission. We estimated the costs associated with each record using previously described methods developed for health administrative data.²¹ For sectors that use global budgets (e.g., hospital, complex continuing care, rehabilitation), we used a top-down approach through case-mix methodology. Sectors where each use has an associated fee payment (e.g., drug costs, physician remuneration) had costs estimated directly. We express all costs in 2018 Canadian dollars, and past costs have been inflated using the healthcare-specific yearly Consumer Price Index reported by Statistics Canada.

Cell sizes with five or fewer patients were suppressed, as per ICES regulations, to protect patient confidentiality.

Statistical analyses

We conducted all statistical analyses using SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC, USA). We present data as mean (standard deviation [SD]) or median [interquartile range (IQR)], as appropriate. The Student’s *t* test (parametric values), Mann–Whitney test (non-parametric values), and ² (for categorical values), were performed to determine between-group differences. We used Kaplan–Meier survival curves to present one-year survival. To identify factors associated with hospital mortality, we used multivariable logistic regression. To determine factors associated with one-year mortality, we used a Cox proportional hazards regression model. We followed the Prognosis Research Strategy (PROGRESS) guidelines when creating our model.²² These guidelines recommend a clinically hypothesis-driven approach for *a priori* selection of all model variables, as opposed to bivariate association testing methods. We ensured the

recommended sample size threshold of ten events per predictor was met.²³ We selected continuous variables (age, time to Impella from admission) and categorical variables (sex, history of CHF, history of CAD, PCI during admission, RRT during admission, VAD during admission, and ECMO during admission) that were most likely to be associated with outcomes in our cohort.

Results

We identified 162 patients receiving Impella for MCS during the study period. Patient characteristics are depicted in Table 1. Mean (SD) age was 59.2 (14.5) yr, and 119 patients (73.5%) were male. Patients were distributed across all income quintiles, and 136 patients (84.0%) resided in an urban setting. The median [IQR] time from hospital admission to Impella initiation was 2 [1–9] days. The most common preadmission comorbidities were hypertension (42.6%), CAD (39.5%), CHF (39.5%), and diabetes mellitus (42.6%).

Table 2 displays short- and long-term patient outcomes. A total of 92 patients (56.8%) died in-hospital, while 86 (53.1%) and 93 (57.4%) died at 30-days and 90-days, respectively. Mortality at one year was 61.7%. The Kaplan–Meier survival curve is depicted in the Figure, and shows a steep decline in survival over the first 30-days after Impella insertion, followed by a relative plateauing of mortality rates.

Median [IQR] hospital length of stay was 15 [4–37] days. With regard to interventions during admission, 100 patients (61.7%) received PCI, while 69 (42.6%) received

RRT. A VAD was implanted in 110 patients (67.9%), and 19 (11.7%) were cannulated for ECMO. Ultimately, fewer than five patients were bridged to cardiac transplant during the index hospitalization. At the time of discharge, 27 patients (38.6% of survivors) were discharged to an independent home setting, while 32 patients (45.7% of survivors) required homecare support, and 11 patients (15.7% of survivors) were discharged to long-term care facilities. Among survivors at discharge, median [IQR] “home time” following discharge at 30-, 90-, and 365 days was 30 [20–30], 90 [74–90], and 320 [259–343] days, respectively.

Comparisons of Impella patients who survived to hospital discharge with those who died prior to discharge are shown in Table 3. No differences were seen in age and sex, but certain preadmission comorbidities were more common among patients who died, including CHF, CAD, hypertension, and history of arrhythmia. Cardiac transplant was associated with survival, but there were no differences in relation to other interventions such as PCI, RRT, VAD, or ECMO. These findings were also seen in the logistic regression model for prediction of hospital mortality (Table 4). History of CHF (odds ratio [OR], 4.61; 95% confidence interval [CI], 1.60 to 13.34) and history of CAD (OR, 6.40; 95% CI, 2.36 to 17.34) were the strongest predictors of hospital mortality. Kaplan–Meier curves comparing survival between patients with and without an existing history of CHF are shown in the eFigure (as ESM). Similarly, Cox regression (eTable 4 in ESM) found that history of CAD (hazard ratio, 2.39; 95% CI, 1.36 to 4.21) was the strongest predictor of one-year mortality.

Figure Kaplan–Meier curve depicting survival in the first year following Impella use among critically ill adult patients in Ontario, Canada (April 2012–March 2019) ($n = 162$)

Table 1 Characteristics of adult patients receiving Impella in Ontario, Canada (April 2012–March 2019) ($n = 162$)

Variable	Value
Sex, n (%)	
Male	119 (73.5)
Female	43 (26.5)
Age, yr, mean (SD)	59.2 (14.5)
Income quintile, n (%)	
Lowest	39 (24.1)
Low	34 (21.0)
Middle	23 (14.2)
High	31 (19.1)
Highest	29 (17.9)
Unknown	6 (3.8)
Rurality, n (%)	
Urban	136 (84.0)
Rural	21 (13.0)
Time from admission to Impella, days, median [IQR]	2 [1–9]
Charlson comorbidity index, median [IQR]	0 [0–1]
Comorbidities prior to admission, n (%)	
Arrhythmia	20 (12.3)
Malignancy	11 (6.8)
Congestive heart failure	64 (39.5)
Chronic obstructive pulmonary disease	12 (7.4)
Coronary artery disease	64 (39.5)
Dementia	*
Diabetes mellitus	46 (28.4)
Hypertension	69 (42.6)
Chronic kidney disease	45 (27.8)
Cerebrovascular disease	8 (4.9)

*Denotes $\leq$ five patients. IQR = interquartile range; SD = standard deviation.

Finally, we evaluated costs in the first year following Impella, which were available for 110 patients (Table 5). Median [IQR] total costs were \$88,397 [32,718–225,628]. Nevertheless, the large majority of these costs were attributable to inpatient care (median [IQR], \$66,529 [22,789–183,165]) and physician billings (median [IQR], \$13,137 [6,633–28,182]). Median costs for complex continuing care, long-term care, rehabilitation, and homecare were \$0. Median costs for outpatient clinics were \$748 [332–2,628].

Discussion

In this population-based cohort analysis of adult patients receiving Impella as MCS, we found that mortality during index hospitalization was high, but did not increase

Table 2 Short- and long-term outcomes of adult patients receiving Impella in Ontario, Canada (April 2012–March 2019, $n = 162$)

Variable	Overall ($n = 162$)
Mortality following Impella initiation, n (%)	
In-hospital	92 (56.8)
30-day	86 (53.1)
90-day	93 (57.4)
1-yr	100 (61.7)
Hospital length of stay, days, median [IQR]	15 [4–37]
Percutaneous coronary intervention during hospitalization, n (%)	100 (61.7)
Renal replacement therapy during hospitalization, n (%)	69 (42.6)
Ventricular assist device during hospitalization, n (%)	110 (67.9)
Extracorporeal membrane oxygenation during hospitalization, n (%)	19 (11.7)
Heart transplant during hospitalization, n (%)	*
Discharge disposition among survivors, n (%)†	
Home (without homecare)	27 (38.6)
Home (with homecare)	32 (45.7)
Long-term care facility	11 (15.7)
Emergency department visit following discharge, n (%)†	
Within 30 days	24 (34.3)
Within 90 days	31 (44.3)
Within 1 year	48 (68.6)
Hospital readmissions following discharge, n (%)†	
Within 30 days	11 (15.7)
Within 90 days	19 (27.1)
Within 1 year	31 (44.3)
Home time following discharge among survivors, median [IQR]†	
Within 30 days of discharge	30 [20–30]
Within 90 days of discharge	90 [74–90]
Within 365 days of discharge	320 [259–343]

†Only includes survivors to discharge ($n = 70$). * = $\leq$ five patients. IQR = interquartile range.

substantially in the subsequent year. Among those who survived to discharge, only a minority were discharged to an independent home setting, with the majority of survivors requiring either homecare support or discharge to a long-term care facility. Both in-hospital and one-year mortality were more strongly predicted by pre-existing patient comorbidities (namely CHF and CAD), rather than interventions occurring during hospitalization, including PCI, RRT, VAD, or ECMO. Finally, use of Impella was associated with significant costs, though these costs largely reflected the index hospitalization, and not downstream costs following discharge. Taken together, this study provides important short- and long-term population-level

Table 3 Comparison of patients receiving Impella who survive to hospital discharge against those who died in hospital

Variable	Surviving to discharge (<i>n</i> = 70)	Died in hospital (<i>n</i> = 92)	<i>P</i> value
Sex, <i>n</i> (%)			0.84
Male	52 (74.3)	67 (72.8)	
Female	18 (25.7)	25 (27.2)	
Age, yr, mean (SD)	58.8	59.4	0.77
Income quintile, <i>n</i> (%)			0.64
Lowest	15 (21.4)	24 (26.1)	
Low	12 (17.1)	22 (23.9)	
Middle	11 (15.7)	12 (13.0)	
High	14 (20.0)	17 (18.5)	
Highest	16 (22.9)	13 (14.1)	
Unknown	*	*	
Rurality, <i>n</i> (%)			0.99
Urban	59 (84.3)	77 (83.7)	
Rural	9 (12.9)	12 (13.0)	
Charlson comorbidity index, median [IQR]	0 [0–2]	0 [0–1]	0.03
Comorbidities, <i>n</i> (%)			
Arrhythmia	*	15–20	<0.01
Malignancy	*	6–11	0.08
Congestive heart failure	13 (18.6)	51 (55.4)	<0.001
COPD	*	7–12	0.47
Coronary artery disease	10 (14.3)	54 (58.7)	<0.001
Diabetes mellitus	12 (17.1)	34 (37.0)	<0.01
Hypertension	13 (18.6)	56 (60.9)	<0.001
Chronic kidney disease	11 (15.7)	34 (37.0)	<0.01
Cerebrovascular disease	*	*	0.74
Time from admission to Impella, days, median [IQR]	4 [2–17]	2 [1–4]	<0.001
Percutaneous coronary intervention, <i>n</i> (%)	41 (58.6)	59 (64.1)	0.47
Renal replacement therapy, <i>n</i> (%)	26 (37.1)	43 (46.7)	0.22
Ventricular assist device during hospitalization, <i>n</i> (%)	48 (68.5)	62 (67.4)	0.87
ECMO during hospitalization, <i>n</i> (%)	9 (12.9)	10 (10.9)	0.70
Heart transplant during hospitalization, <i>n</i> (%)	*	*	<0.01

*Denotes $\leq$ five patients. COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; IQR = interquartile range; SD = standard deviation.

data regarding outcomes following the use of Impella for MCS.

Overall use of Impella in the United States has been increasing exponentially, despite minimal evidence supporting its use over IABP or other types of MCS for patients with high-risk PCI.¹⁰ Less evidence exists supporting the use of Impella in cases of cardiogenic shock. The majority of investigations into the efficacy of Impella have been observational in nature, and recent studies suggest an association between Impella use and worse outcomes among patients, particularly when compared with IABP, even after adjusting for severity of illness.^{10,24,25} Our study shows high rates of hospital

mortality among patients receiving Impella. Nevertheless, we also found relatively minimal increase in mortality at one year. This suggests patients with cardiogenic shock who receive Impella and survive their initial hospital stay are likely to be alive after one year. This finding has previously been shown in patients receiving IABP,²⁶ as well as those receiving other types of MCS, such as ECMO.¹⁵ We found that Impella patients were commonly bridged to VAD, but only a few ultimately received cardiac transplantation, at rates much lower than similar patients receiving ECMO.¹⁵ Lastly, in contrast to patients receiving ECMO,¹⁵ we found that only a minority of patients receiving Impella were discharged to an independent home

Table 4 Multivariable logistic regression for prediction of hospital mortality

Parameter	Odds ratio	95% confidence interval
Age (per 1 yr)	0.99	0.97 to 1.03
Female sex	1.54	0.62 to 3.79
History of congestive heart failure	4.61	1.60 to 13.34
History of coronary artery disease	6.40	2.36 to 17.34
Time from admission to Impella (per 1 day)	0.90	0.86 to 0.95
Percutaneous coronary intervention during admission	1.18	0.50 to 2.77
Renal replacement therapy during admission	1.62	0.71 to 3.73
Ventricular assist device during admission	0.97	0.42 to 2.28
Extracorporeal membrane oxygenation during admission	0.86	0.25 to 2.91

setting. Nevertheless, median “home time” was relatively high among survivors, suggesting that the majority of these patients are at least able to return to a private residence. Future randomized studies may provide better insight into the efficacy of the Impella device, including impact on functional outcome.

Prediction of survival following Impella is an important area of research, and has the potential to aid in selection of patients most likely to benefit from this technology.²⁷ Interestingly, our multivariate models for both in-hospital mortality and one-year mortality found that the greatest impact on survival came from presence of preadmission CHF and CAD, though the severity of these disease states could not be identified from our databases. Interestingly, in-hospital interventions were not associated with mortality following Impella use. Survival from cardiogenic shock has been frequently associated with revascularization through PCI^{28–30}; however, we found no association between revascularization and mortality in this cohort. Similarly, RRT has been associated with worse outcomes in cardiogenic shock,³¹ but again was not found to be associated with mortality in this study. This highlights the importance of patient selection in MCS for cardiogenic shock, and suggests that patients with pre-existing comorbidities may be at a higher risk of death following Impella use. As Impella use grows, derivation of predictive models would be helpful to assist clinicians in identifying optimal candidates for this technology.

Finally, given concerns of significant hospital-level costs associated with Impella,¹⁰ we evaluated patient-level costs both in the short- and long-term. Impella use was associated with significant costs, comparable to

Table 5 One-year costs following admission of adult patients requiring Impella in Ontario, Canada (April 2012–March 2018) (*n* = 110)

	Mean (SD) costs	Median [IQR] costs
Acute care sectors		
Inpatient	127,026 (152,066)	66,529 [22,789–183,165]
Emergency department	682 (651)	583 [265–943]
Continuing care sectors		
Complex continuing care	61 (637)	0 [0–0]
Long-term care	0 (0)	0 [0]
Rehabilitation	1,270 (4,499)	0 [0–0]
Homecare	1,202 (3,030)	0 [0–416]
Outpatient care sectors		
Outpatient clinics	2,215 (3,022)	748 [332–2,628]
Laboratory (OHIP)	147 (363)	0 [0–155]
Drugs (Ontario drug benefit program)	1,295 (3,067)	0 [0–1,128]
Physician billings†	19,406 (17,594)	13,137 [6,633–28,182]
Total costs	156,775 (171,714)	88,397 [32,718–225,628]

All values in 2018 Canadian dollars. †Includes both inpatient and outpatient physician billings. IQR = interquartile range; OHIP = Ontario Health Insurance Plan; SD = standard deviation.

ECMO use in Ontario,¹⁵ and IABP use in Europe.³² The median total costs for patients receiving Impella, while high, are much lower than the 90th percentile of high-costs for patients in Canadian critical care settings,³³ and are significantly less than other high-cost critical care populations, such as patients with subarachnoid hemorrhage.³⁴ Importantly, the costs associated with Impella use largely reflect the costs of the inpatient hospitalization. The mean cost of the Impella 5.0 alone in Ontario is \$36,000.⁶ This is a key distinction, as many critically ill populations have been found to not only consume healthcare resources and costs during their initial hospitalization, but also downstream in the months and years following discharge.^{35,36} We found that Impella survivors incur relatively fewer costs following discharge, likely a reflection of their relatively lower age and comorbidity burden compared with other survivors of critical illness.

We used robust population-level data to identify long-term outcomes and costs associated with Impella use in Ontario, and provide novel and important data necessary to evaluate the impact of this therapy. Nevertheless, this study does have limitations. Most importantly, we are limited in the granularity of data available in our population-based databases. Specifically, we lack data related to

comorbidities (including the severity of existing CHF and CAD, or specific arrhythmias), severity of illness, indications for Impella use, and discernable costs (such as costs covered privately by patients). While the indication for Impella may not be clear, its use in Ontario is largely reserved for cardiogenic shock over other conditions (such as high-risk PCI),⁶ and the severity of illness in our population is evidenced by the high proportion of VAD, RRT, and ECMO use in our cohort. Secondly, while this is one of the largest Impella studies published to date, the complexity of our regression models was limited by the sample size. Larger studies are required to derive models that can more accurately predict optimal patient selection. Third, the included patients represent a highly selected population, and readers should exercise caution in extending the findings to all patients with cardiogenic shock, or using the results to understand the efficacy of Impella—a task best suited to a randomized clinical trial. Fourth, Impella use is associated with significant adverse events,^{8,10} and we were unable to capture the incidence of such adverse events in our database. Finally, our patients were gathered from seven highly-specialized tertiary centres from a single jurisdiction, and existing data shows inter-facility variability in outcomes following Impella use, based upon the volume of use at individual centres.¹⁰

Conclusion

This population-based cohort study shows high hospital mortality (56.8%) among adult cardiogenic shock patients receiving Impella, with only a small incremental increase at one year. Only a minority of patients receiving Impella were ultimately able to be discharged to an independent home setting, with most survivors requiring homecare assistance, or long-term care residency. In-hospital and one-year Impella mortality were associated with pre-existing comorbidities (namely CHF and CAD). Finally, Impella patients accrued significant inpatient costs, though these costs were less than typical high-cost populations, and these patients had relatively minimal healthcare-associated costs in the one year following Impella initiation. This work provides novel data regarding the long-term mortality and costs of cardiogenic shock patients receiving Impella for MCS.

Author contributions Shannon M. Fernando, Peter Tanuseputro, and Kwadwo Kyeremanteng conceived the study. Shannon M. Fernando, Danial Qureshi, Peter Tanuseputro, Robert Talarico, Benjamin Hibbert, Bram Rochweg, and Kwadwo Kyeremanteng participated in study design. Danial Qureshi and Robert Talarico gathered the data and performed data analyses. All authors interpreted the data analyses. All authors co-wrote and revised the manuscript for

intellectual content. All authors agree to be accountable for all aspects of the work.

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