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REPORTS OF ORIGINAL INVESTIGATIONS

Long-term survival and resource use in critically ill cardiac surgery patients: a population-based study

Survie à long terme et utilisation des ressources par les patients chirurgicaux cardiaques dans un état critique : une étude basée sur la population

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Abstract

Purpose *Most cardiac surgery patients recover well; a substantial minority become critically ill after surgery. The epidemiology of critical illness after cardiac surgery is poorly described. We measured the association of prolonged critical illness with long-term survival and resource use after cardiac surgery.*

Methods *This was a historical population-based cohort study in Ontario, Canada (2002-2013), of adult cardiac surgery patients. Validated methods were used to measure postoperative intensive care unit (ICU) length of stay (LOS). We categorized patients into short (0-2 day), moderate (3-9 day), and long (10+ day) ICU LOS groups. The adjusted associations of ICU LOS with one-year survival (primary outcome) and costs, hospital readmissions, and institutional discharge were measured using multilevel, multivariable regression. Pre-specified sensitivity analyses were performed.*

Results *We included 111,740 patients having their first cardiac surgery during the study period who survived ≥ ten postoperative days. Most patients had a short ICU LOS (75.9%); 20.9% and 3.3% had moderate or long ICU LOS, respectively. The short-stay one-year mortality rate was 2.1%. Longer ICU LOS was independently associated with*

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decreased one-year survival (moderate LOS: hazard ratio [HR], 1.79; 95% confidence interval [CI], 1.6 to 1.94; long LOS: HR, 8.66; 95% CI, 7.93 to 9.44). Sensitivity analyses supported the findings of the primary analysis. Secondary outcomes were independently associated with longer ICU LOS. Long ICU LOS patients occupied 30% of all ICU bed days, and 55% died or were discharged to an institution.

Conclusion *Prolonged ICU LOS after cardiac surgery is associated with decreased 1-year survival and increased healthcare resource use.*

Résumé

Objectif *La majorité des patients chirurgicaux cardiaques récupère bien, mais une minorité importante d'entre eux présente un état critique après la chirurgie. L'épidémiologie de la phase critique faisant suite à la chirurgie cardiaque est mal connue. Nous avons mesuré l'association entre, d'une part, l'état critique prolongé et, d'autre part, la survie à long terme et l'utilisation des ressources après chirurgie cardiaque.*

Méthodes *Il s'est agi d'une étude de cohorte historique basée sur la population de patients chirurgicaux cardiaques de la province d'Ontario (Canada, de 2002 à 2013). Des méthodes validées ont été utilisées pour mesurer la durée de séjour en unité de soins critiques (USC) postopératoires. Nous avons classé les patients en fonction de leur durée de séjour (DS) dans l'USC : groupe à DS courte (0 à 2 jours), groupe à DS modérée (3 à 9 jours) et groupe à DS longue (10 jours et plus). Les associations ajustées de la DS en USC avec la survie à un an (critère d'évaluation principal) et les coûts, les réhospitalisations et les transferts vers des soins de longue durée ont été mesurées à l'aide d'une régression multifactorielle à plusieurs niveaux. Des analyses préspécifiées de sensibilité ont été effectuées.*

Résultats *Nous avons inclus 111 740 patients ayant eu leur première chirurgie cardiaque au cours de la période d'étude et ayant survécu ≥ dix jours dans la période postopératoire. La DS en USC de la majorité des patients a été courte (71,7 %) tandis que la DS a été modérée ou longue pour, respectivement, 23,4 % et 4,9 % des patients. Le taux de mortalité à un an après DS courte était de 2,1 %. Une DS plus longue en USC a été associée de manière indépendante à une baisse de la survie à un an (DS modérée : rapport de risque [RR], 1,79; intervalle de confiance [IC] à 95 % : 1,6 à 1,94; DS longue : RR, 8,66; IC à 95 % : 7,93 à 9,44). Les analyses de sensibilité ont confirmé les constatations de l'analyse principale. Les critères d'évaluation secondaires ont été associés de manière indépendante à une DS plus longue en USC. Les patients ayant eu une DS longue en USC ont occupé 30 % des journées d'hospitalisation en USC et 55 % d'entre eux sont décédés ou ont obtenu un congé vers un établissement de soins de longue durée.*

Conclusion *Une DS prolongée en USC après chirurgie cardiaque est associée à une baisse de la survie à 1 an et à une augmentation de l'utilisation des ressources de soins de santé.*

More than 500,000 patients undergo cardiac surgery each year,[1,2] with the majority of cardiac surgery occurring in people over 65 years of age.[3] As the population continues to grow and age, the demand for cardiac surgery is expected to increase also.[3] Many patients have an uncomplicated recovery; however, up to a third of patients experience major postoperative morbidity with organ dysfunction requiring life-sustaining therapies in an intensive care unit (ICU) setting.[4] Unfortunately, this critical illness and life-supporting therapies—started as a short-term bridge to recovery—may lead to poor long-term outcomes. Since advanced age is an independent predictor of post-cardiac surgery critical care use,[5] the need for critical care services will likely escalate and consume an even greater proportion of healthcare system resources.

To date, there are few data that comprehensively examine critical illness following cardiac surgery. Existing data have been limited by single-centre enrolment, small sample sizes, focus on single organ failure, and short-term follow-up.[4,6,7] Furthermore, the majority of data describing long-term outcomes of critically ill patients are derived from mixed medical/surgical intensive care units, where sepsis and respiratory failure are the most common non-cardiac reasons for ICU admission.[8,9] For the cardiac surgical population, it is inadequate to extrapolate from these data, as baseline patient characteristics, postoperative pathophysiologies, and the potential benefit of improved cardiac function are substantially different following cardiac surgery compared with other critically ill patients

Population-based epidemiologic studies can inform patients, clinicians, and policymakers to support decision making and plan for current and future ICU demands. Therefore, our objective was to comprehensively describe long-term mortality and resource utilization following postoperative critical care stays in a universal healthcare system in Ontario, Canada.

Methods

Following approval by the Sunnybrook Health Sciences Centre Research Ethics Board, we conducted a population-based cohort study in Ontario, Canada, where health services are publicly funded and records are collected in administrative data sets using standardized methods.[10,11] Need for written consent was waived because of the routinely collected and de-identified nature of all data, which were linked deterministically using encrypted patient-specific identifiers at the Institute for Clinical Evaluative Sciences (ICES). Data sets used for the study included: the Discharge Abstract Database, which captures all hospitalizations; the Ontario Health Insurance Plan database, which captures physician service claims; the National Ambulatory Care Reporting System, which captures all emergency department visits; the Continuing Care Reporting System, which records details of long-term and respite care; and the Registered Persons Database, which captures all death dates. The analytic data set was created and analyzed by an independent analyst using data normally collected at ICES. This manuscript is reported using appropriate guidelines.[12,13]

Cohort

We identified all adults in Ontario having one of the five most common cardiac surgical procedures between April 2002 (which was the date of introduction for the Canadian Classification of Interventions system to identify surgical procedures) and March 2013 (the most recent date for which all data were complete at the time of analysis). We did not include transcatheter valve insertions. The annual number of cases of each procedure per year was cross-referenced with prospectively monitored provincial reports to ensure accuracy.[14] Included procedures were: isolated coronary artery bypass graft (CABG), isolated aortic valve repair or replacement, combined CABG and aortic valve repair or replacement, combined CABG and mitral valve repair or replacement, or multivalve surgery (codes are provided in Table 1A, available as Electronic Supplementary Material). We included patients having emergency and elective surgery.

Exposure

Administrative data in Ontario have $\geq$ 98% positive predictive value and > 99% negative predictive value in accurately identifying ICU care.[15] Our main exposure, ICU length of stay (LOS), was calculated using these methods. Length of stay was defined as the date of each patient's first ICU discharge minus their date of postoperative admission. We categorized ICU LOS into three mutually exclusive categories: ICU LOS $\leq$ two days; ICU LOS three to nine days; ICU LOS $\geq$ ten days. Boundaries were informed by clinical expertise and systematic reviews of prolonged ICU length of stay and outcomes after cardiac surgery.[16] Although most studies used a binary definition of prolonged LOS, the cutoff values varied extensively. Therefore, our three-level variable reflected typical lower and upper values used in previous studies and was supported by clinical experience.

Because patients who died within nine days of surgery would not have been able to have an ICU LOS of ten or more days, these patients were excluded from all analyses.

Outcomes

The primary outcome was death within 365 days of surgery, identified from vital statistics (the gold standard definition of mortality in Ontario). Secondary outcomes included costs of care incurred by the publicly funded healthcare system (calculated using established and validated patient-level costing algorithms,[17] standardized to 2014 Canadian dollars), institutional discharge (defined as a non-home hospital discharge destination that was not an acute care transfer), and hospital readmission within 30 days of discharge (identified as the creation of a new record in the discharge abstract database within 30 days of discharge from the index hospitalization).

Covariates

Demographics were identified from the Registered Persons Database. Validated algorithms were used to identify all Elixhauser comorbidities based on International Statistical Classification of Diseases and Related Health Problems (ICD)-9 and ICD-10 diagnostic identified in the three years preceding the index admission.[18] Heart failure was identified using a validated algorithm.[19] Acute care hospitalizations and emergency department visits in the year before the index hospital admission were recorded. We identified coronary stents inserted in the year before surgery, previous sternotomies, and each patient's American Society of Anesthesiology (ASA) Score from physician billing. We also recorded whether each patient was in the ICU prior to surgery, the length of their preoperative hospital stay, and the urgency of their index hospital admission (elective *vs* urgent).

Analysis

All patient, admission, and surgical characteristics were compared between each category of ICU LOS using Chi-square tests. All analyses were performed using SAS v9.4 (SAS Institute, Cary, NC, USA).

Crude and adjusted analyses were performed for each outcome with ICU LOS category as the exposure of interest (0-2 day category was the reference for all analyses). Adjusted analyses employed multilevel multivariable regression models that accounted for clustering at the hospital level. Mortality was analyzed

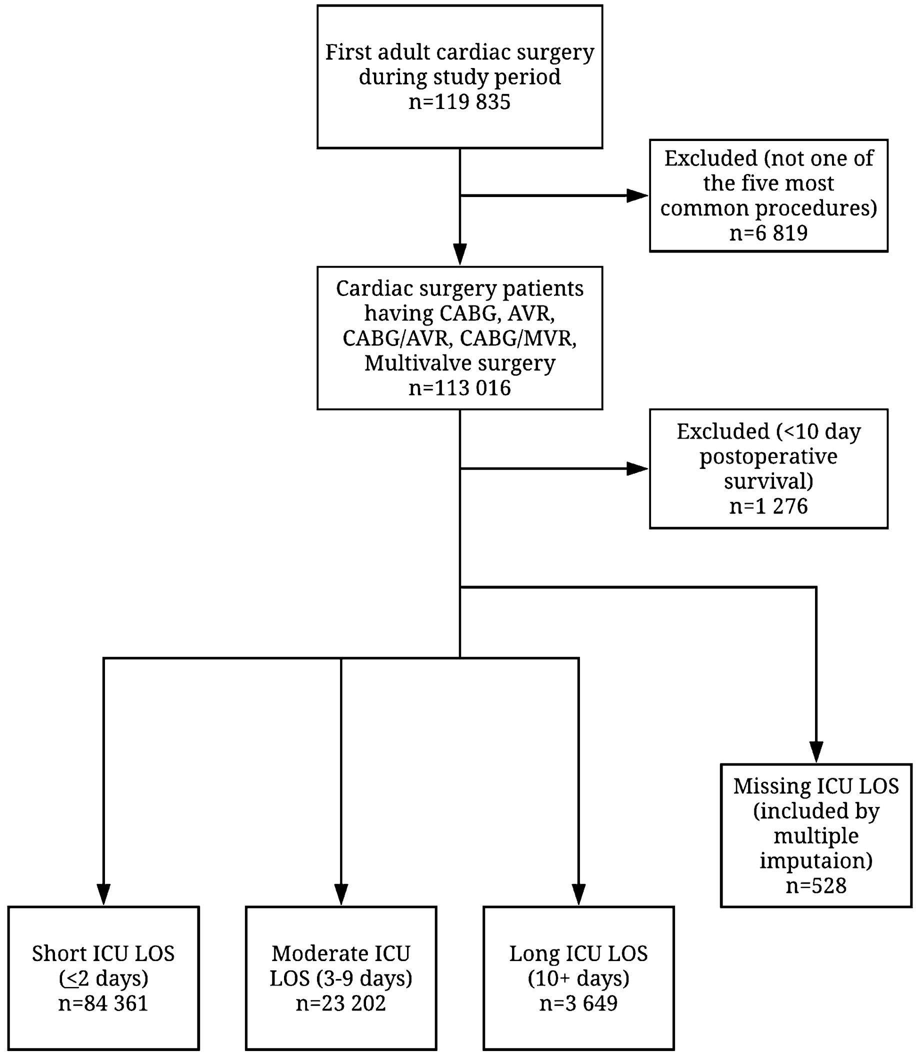

Fig. 1 Cohort creation flow diagram. AVR = aortic valve repair or replacement; CABG = coronary artery bypass grafting; MVR = mitral valve repair or replacement

using proportional hazards regression, and the proportional hazards assumption was assessed using log-negative-log plots. Cost data were analyzed using generalized linear mixed models with a gamma distribution and a log link.[20] All other outcomes were binary in nature and were therefore analyzed using generalized linear mixed models with a binary response distribution. Discharge disposition and hospital readmission analyses were limited to patients who were discharged alive from the index hospitalization.

All adjusted models accounted for covariates based on a priori specified clinical and epidemiologic knowledge of factors that could confound the association between the need for a longer ICU LOS and outcomes. The variables used and their associated formats are provided in the results tables.

Missing data

All outcome data were complete. Exposure data (ICU LOS) were missing for 528 (0.46% of cohort). In our outcome model these missing data were imputed using predictive mean matching methods with PROC MI in SAS based on all covariate data used in our primary and secondary analyses. Analysis of the five imputed data sets was done using PROC MIANALYZE. Linear regression using the same covariates was used to impute ICU LOS for calculation of descriptive statistics. Covariate data were complete except for income quintile (0.4%) and rural residency status (0.1%). These values were imputed with the most common values (income quintile 3 and not rural, respectively).

Sensitivity and subgroup analyses

We performed several prespecified sensitivity analyses. First, we determined the best fitting continuous representation of our ICU LOS exposure using fractional polynomials.[21] The identified polynomial transformation (square root) was then entered into our multilevel multivariable survival model as a continuous term in

Table 1 Patient characteristics by intensive care unit length of stay category

Characteristic	0 to 2 days (*n* = 84,765)*	3 to 9 days (*n* = 23,309)*	10+ days (*n* = 3,666)*	*P* value
Demographics				
Age				
< 50	7.6	4.9	4.7	< 0.001
50-59	21.5	14.4	10.8	
60-69	33.4	29.0	25.3	
70-79	29.9	37.5	42.0	
≥ 80	7.6	14.2	17.2	
Female	23.1	31.2	32.8	< 0.001
Income quintile				
Lowest	18.3	21.3	22.0	< 0.001
2	20.7	22.4	22.7	
3	20.4	19.5	19.5	
4	20.6	18.8	18.3	
Highest	20.0	18.1	17.5	
Rural	15.3	17.6	14.3	< 0.001
Comorbidities				
ASA < 4	9.8	7.4	7.5	< 0.001
Alcohol abuse	1	1.5	2.2	< 0.001
Atrial fibrillation	16.7	30.2	40.9	< 0.001
Blood loss anemia	7.2	13.2	23.0	< 0.001
Cardiac valvular disease	21.2	34.5	44.2	< 0.001
Cerebrovascular disease	4.2	7.2	16.6	< 0.001
Chronic renal disease	4.7	10.9	17.9	< 0.001
Coagulopathy	3.2	7.9	17.8	< 0.001
Deficiency anemia	0.5	0.8	1.4	< 0.001
Dementia	0.2	0.6	0.8	< 0.001
Depression	1.2	2.0	4.1	< 0.001
Diabetes with complications	21.6	27.7	31.0	< 0.001
Diabetes without complications	13.8	15.8	19.6	< 0.001
Dialysis	1.1	2.5	4.6	< 0.001
Drug abuse	0.3	0.4	0.7	< 0.001
Chronic obstructive pulmonary disease	5.7	9.5	13.8	< 0.001
Hypertension with complications	2.6	5.1	8.8	< 0.001
Hypertension without complications	46.6	51.1	50.0	< 0.001
Heart failure	13.2	28.6	46.5	< 0.001
Hemiplegia or hemiparesis	0.3	0.8	3.1	< 0.001
Liver disease	0.7	1.5	3.3	< 0.001
Metastatic solid tumour	0.3	0.4	0.7	< 0.001
Obesity	3.4	4.8	5.0	< 0.001
Peripheral vascular disease	7.4	11.7	16.7	< 0.001
Primary malignancy	3.6	4.5	5.5	< 0.001
Psychoses	0.3	0.4	0.4	0.0011
Disease of the pulmonary circulation	1.5	4.2	8.2	< 0.001
Rheumatologic disease	0.7	1.0	1.2	< 0.001
Peptic ulcer disease	1.3	2.0	3.6	< 0.001
Venous thromboembolism	0.4	0.9	2.7	< 0.001
Weight loss	0.3	0.6	1.3	< 0.001
Cardiac stent in previous year	3.1	2.8	3.5	0.03

Table 1 continued

Characteristic	0 to 2 days (*n* = 84,765)*	3 to 9 days (*n* = 23,309)*	10+ days (*n* = 3,666)*	*P* value
Acute hospitalization in previous year	28.2	34.1	38.3	< 0.001
ED visit in previous year	46.8	53.9	56.0	< 0.001
Surgical factors				
Elective admission	53.7	46.7	39.3	< 0.001
Procedure				
Isolated CABG	78.8	66.0	52.0	< 0.001
Combined CABG/AVR	8.1	14.0	18.7	
Isolated AVR	9.5	9.8	8.8	
CABG + mitral surgery	0.8	2.7	6.3	
Multi-valve surgery	2.8	7.5	14.2	
Previous sternotomy	0.1	0.2	0.5	< 0.001
Missing exposure status	*n* = 404 (0.5)	*n* = 107 (0.5)	17 (0.5)	0.9

ASA = American Society of Anesthesiology Society; AVR = aortic valve repair or replacement; CABG = coronary artery bypass grafting; ED = emergency department; ICU = intensive care unit. *Individuals with missing intensive care unit length of stay data had the missing value imputed using regression (total *n* = 528)

addition to the covariates used in our primary analysis. Next, to assess the impact of imputing missing ICU LOS data, we re-ran our primary analysis including only people with non-missing ICU LOS.

To assess for effect modification in pertinent subgroups, we created a series of regression models with an interaction term included that multiplied our primary exposure by the postulated effect modifier. The effect modifiers tested included admission urgency, surgery type, sex, age, and year of surgery. During peer review heart failure was also suggested as an effect modifier. Where the interaction term was found to be statistically significant, we calculated the effect size at each level of the effect modifier.

Post hoc, we did two additional cost analyses suggested in peer review to determine the impact of preoperative resource use trajectories on cost outcomes after surgery and to differentiate between in-hospital and post-discharge costs. These are described in Table 2A (available as Electronic Supplementary Material).

Results

We identified 119,835 cardiac surgery patients from 11 centres performing cardiac surgery in Ontario during the study period, of whom 111,740 (93.2%) had one of the five most common procedures and lived at least ten days after surgery (Fig. 1); 1,276 (1.1%) patients having an eligible surgery died prior to postoperative day 10. Overall, study subjects occupied 291,366 total ICU bed days, with most individuals (75.9%) having an ICU LOS of two days or less, 20.9% having an ICU stay between three to nine days, and 3.3% having an ICU LOS of ten days or longer. The

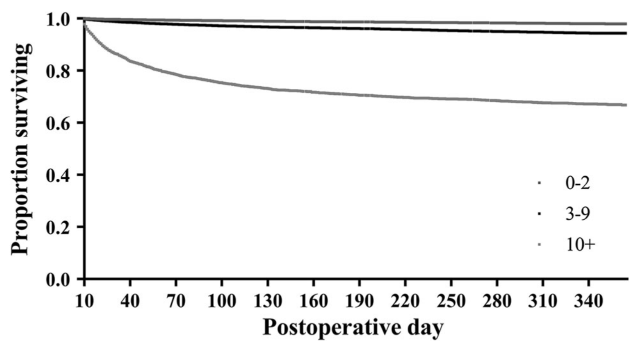

Fig. 2 Crude survival curves by intensive care unit (ICU) length of stay category. This figure shows the proportion of individuals in each ICU length of stay category who were still alive on each day in the first postoperative year

mean (standard deviation [SD]) ICU LOS was 2.7 (6.0) days. The longest ICU LOS group occupied 86,487 ICU days (30% of all ICU days), while the short-stay group occupied 103,575 ICU days (36% of total). Most baseline characteristics differed significantly between categories of postoperative ICU LOS, with longer LOS patients tending to be older, less likely to have had an isolated CABG, more likely to have had urgent surgery, and more likely to be in ICU prior to their operation (Table 1).

Intensive care unit LOS and one-year survival in those surviving at least ten days after surgery

In the year after surgery, 4,286 people died (3.8%). Prior to covariate adjustment, there were significant differences between ICU LOS categories and mortality; 2.1% of short ICU stay patients died in the year after surgery compared with 5.7% of moderate- and 33.2% of long-stay patients.

Table 2 Multilevel, multivariable adjusted survival model

Covariate	HR	95% CI
Main exposure		
ICU length of stay ≤ 2 days	Reference	
3-9 days	1.79	1.60-1.94
≥ 10 days	8.66	7.93-9.44
Demographics		
Age (years) < 50	Reference	
50-59	1.10	0.92-1.31
60-69	1.59	1.37-1.84
70-79	2.40	2.06-2.80
≥ 80	3.82	3.26-4.48
Female (*vs* male)	1.16	1.10-1.22
Income quintile 1 (lowest)	Reference	
2	0.95	0.89-1.02
3	0.94	0.87-1.01
4	0.93	0.87-0.99
5 (highest)	0.85	0.77-0.93
Rural (*vs* not rural)	0.94	0.87-1.02
Comorbidities		
ASA score < 3	Reference	
3	0.57	0.45-0.72
4	0.86	0.76-0.98
5	1.97	1.72-2.26
Alcohol abuse	1.15	0.97-1.37
Atrial fibrillation	0.94	0.87-1.01
Blood loss anemia	1.09	1.01-1.18
Cardiac valvular disease	0.98	0.85-1.12
Cerebrovascular disease	1.42	1.32-1.53
Chronic renal disease	1.41	1.28-1.56
Coagulopathy	1.26	1.14-1.39
Deficiency anemia	1.11	0.92-1.34
Dementia	1.20	0.93-1.54
Depression	1.00	0.86-1.17
Diabetes with complications	1.27	1.17-1.37
Diabetes without complications	1.03	0.95-1.11
Dialysis	1.73	1.52-1.96
Drug abuse	1.08	0.76-1.53
Chronic obstructive pulmonary disease	1.31	1.21-1.40
Hypertension with complications	0.95	0.84-1.07
Hypertension without complications	0.98	0.91-1.05
Heart failure	1.80	1.66-1.96
Hemiplegia or hemiparesis	1.15	0.94-1.40
Liver disease	1.90	1.63-2.22
Metastatic solid tumour	1.53	1.14-2.05
Obesity	0.99	0.88-1.11
Peripheral vascular disease	1.44	1.34-1.55
Primary malignancy	1.50	1.37-1.65
Psychoses	1.05	0.67-1.66
Disease of the pulmonary circulation	1.23	1.07-1.40
Rheumatologic disease	1.56	1.32-1.85
Peptic ulcer disease	1.25	1.10-1.42
Venous thromboembolism	1.04	0.80-1.36
Weight loss	1.23	0.95-1.59
Cardiac stent in previous year	1.03	0.88-1.20
Acute hospitalization in previous year	1.01	0.93-1.09
ED visits in previous year 0	Reference	
1	0.98	0.91-1.04
>1	1.10	1.01-1.19
Surgical factors		
Urgent admission (*vs* elective)	1.46	1.27-1.68
Preoperative LOS 0 days	Reference	
1-2 days	0.72	0.62-0.82
≥ 3 days	0.73	0.63-0.86
In ICU before surgery	1.30	1.19-1.43
Isolated CABG	Reference	
Combined CABG/AVR	1.79	1.40-2.29
Isolated AVR	1.54	1.31-1.80
CABG + mitral surgery	1.26	1.06-1.50
Multi-valve surgery	1.65	1.37-1.98
Previous sternotomy	1.09	0.67-1.76
Year of surgery 2002-03	Reference	
2003-04	0.98	0.87-1.10
2004-05	1.16	1.02-1.32
2005-06	1.11	0.96-1.28
2006-07	0.99	0.84-1.17
2007-08	1.04	0.91-1.18
2008-09	0.98	0.85-1.13
2009-10	0.97	0.82-1.15
2010-11	0.99	0.86-1.15
2011-12	0.97	0.83-1.13
2012-13	0.95	0.81-1.12
2013-14	0.87	0.74-1.02

ASA = American Society of Anesthesiology Society; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CI = confidence interval; ED = emergency department; HR = hazard ratio; ICU = intensive care unit

Compared with short LOS patients, moderate LOS patients had an almost three-fold decrease in survival (unadjusted hazard ratio [HR], 2.79; 95% CI, 2.60 to 3.00), while long-LOS patients had a 20-fold decrease (unadjusted HR, 20.16; 95% CI, 18.73 to 21.71). In-hospital mortality rates were 0.3% (0-2 day ICU LOS), 1.5% (3-9 day ICU LOS), and 25.5% (10+ day ICU LOS). Crude survival curves are provided in Fig. 2.

Following multilevel multivariable adjustment, ICU LOS category continued to be significantly associated with survival ($P < 0.001$ for all comparisons). Compared

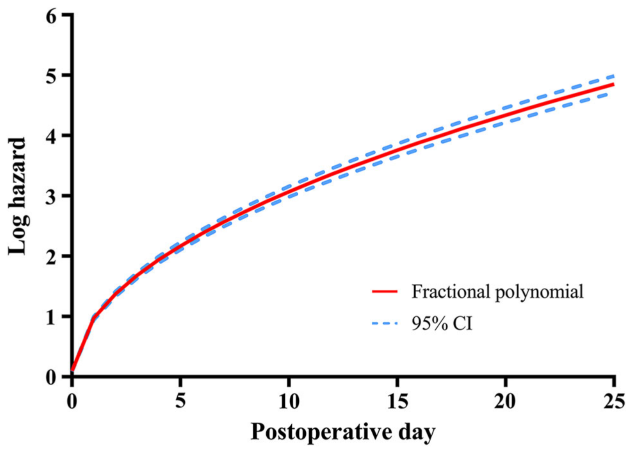

Fig. 3 Adjusted association between the square root of intensive care unit (ICU) length of stay (LOS) and hazard of mortality. To generate this figure we identified the best fitting continuous representation of ICU LOS using fractional polynomial analysis, which was the square root function. We then calculated the adjusted log hazard of mortality (compared with someone with an ICU LOS of 0.01 days; any patient with an ICU LOS < one day was set to 0.01 days) for each postoperative day over the first 25 days after surgery

with patients who stayed in ICU ≤ two days, patients with an ICU LOS of three to nine days were 80% more likely to die in the year after surgery (adjusted HR, 1.79; 95% CI. 1.60 to 1.94), while patients who required ten or more days of ICU care after cardiac surgery had more than an eight-fold increase in mortality risk (adjusted HR, 8.66; 95% CI, 7.93 to 9.44). The fully adjusted model is presented in Table 2.

Our sensitivity analysis of the continuous association of ICU LOS (expressed as the square root of ICU LOS) and survival was also significant ($P < 0.001$). Figure 3 illustrates the hazard of one-year mortality by ICU LOS across the first 25 postoperative days. After an initial steep rise in risk of death with each excess day in ICU, there was an inflection point at two days, after which the slope of the curve decreased slightly, and then a second inflection at approximately eight days of ICU stay. After this point there appeared to be a linear association between mortality risk and ICU LOS up to the 25th postadmission day.

When the primary analysis was limited to patients with non-missing ICU LOS, adjusted effect measures were similar to those in the primary analysis, which included imputed LOS values (moderate LOS *vs* short: adjusted HR, 1.80; 95% CI, 1.63 to 1.98; long LOS *vs* short: adjusted HR, 8.74; 95% CI, 7.58 to 10.08).

Secondary outcomes

One-year total healthcare costs also differed substantially between ICU LOS categories, as did readmission rates and rates of institutional discharge. Following multilevel multivariable adjustment all secondary outcomes continued to be significantly associated with ICU LOS (Table 3).

Sensitivity analyses

The impact of length of ICU LOS on one-year survival differed significantly across all postulated effect modifiers (admission urgency, surgery type, age, heart failure, and year of surgery all $P < 0.001$) except for sex ($P = 0.2$); a full description of all effect modification is provided in Figure A (available as Electronic Supplementary Material). In summary, one-year survival was most significantly impacted by long ICU LOS after isolated CABG (adjusted HR, 10.82; 95% CI, 9.16 to 12.74), in younger patients (age < 50: adjusted HR, 15.54; 95% CI, 10.88 to 22.02), in people without heart failure (adjusted HR, 15.38; 95% CI, 13.70 to 17.24), and after elective surgery (adjusted HR, 11.18; 95% CI, 9.50 to 13.16). No clear trend was apparent across study years.

Discussion

In this population-based cohort study, patients who required ten or more days in ICU after cardiac surgery were substantially more likely to die in the year after surgery. Long-stay patients also consumed significantly more healthcare resources. This included 30% of all ICU bed days (despite comprising less than 5% of the total cardiac surgery population) and an additional $100,000 per person in health system spending compared with patients in ICU for two or fewer days. Of the patients who were discharged alive from hospital, prolonged ICU length of stay patients also had a substantial loss of independence, resulting in a 7.5-fold increase in their odds of discharge to an institution. Overall, more than 55% of long ICU LOS patients either died in hospital or were institutionalized at discharge.

Temporal trends show that ICU stays are getting longer.[22] Therefore, a better understanding of chronic critical illness (CCI, where patients survive critical illness only to become dependent on one or more life supportive therapies)[23] is required. Our findings suggest that cardiac surgery patients who require prolonged critical care (which is a proxy for CCI), compared with prolonged stay mixed critically ill populations, have higher one-year mortality rates (33% *vs* 14-22%) and decreased adjusted relative one-year survival (eight-fold decrease *vs* 1.0-1.2-fold decrease).[9] The relative survival difference is partly driven by the increased absolute overall one-year mortality rate in mixed critical care compared with cardiac settings (15% *vs* 4%).[9] This highlights the

Table 3 Crude and adjusted secondary study outcomes by ICU LOS category

Outcome	ICU LOS 0-2 days n = 84,765	ICU LOS 3-9 days n = 23,309	ICU LOS 10+ days n = 3,666	Unadjusted relative association‡ 95% CI		Adjusted relative association‡ 95% CI	
				3-9 *vs* 0-2	10+ *vs* 0-2	3-9 *vs* 0-2	10+ *vs* 0-2
1-year costs of care (median)†	29,020	40,590	120,200	1.27	3.06	1.27	3.06
IQR	23,979-38,112	29,904-61,089	75,436-188,673	1.26 to 1.29	2.99 to 3.14	1.23-1.29	2.99-3.13
Institutional discharge (*n*)*	3,273	2,038	805	2.47	11.80	1.61	7.51
%	3.9	9.1	32.4	2.33 to 2.62	10.78 to 12.93	1.51 to 1.72	6.70 to 8.42
Readmission (*n*)*	9,796	4,557	1,422	1.59	2.03	1.25	1.28
%	11.4	19.2	39.2	1.52 to 1.66	1.83-2.25	1.19 to 1.31	1.14 to 1.43

ICU = intensive care unit; LOS = length of stay; IQR = interquartile range. *Institutional discharge and readmission analyses limited to people discharged alive from hospital; therefore, denominators were - 0-2 day 83608, 3-9 day 22294, 10+day 2479; †2014 Canadian dollars; ‡cost analyses expressed as incidence rate ratios, institutional discharge and readmissions as odds ratios

important distinction between general critical care and cardiothoracic critical care.[24] Additionally, of prolonged ICU LOS patients in our study who were discharged alive from hospital, 32% were discharged to an institution, and 40% of those discharged home were readmitted to hospital. Therefore, even without being able to measure moderate functional disability that may be managed at home, a majority of people who require a prolonged ICU LOS after cardiac surgery will be dead or institutionalized in the year after surgery. For those discharged home, acute health issues are likely to continue. These findings should be discussed with patients (or more realistically their family and support network) as acute critical illness transitions toward chronic ICU stays. Furthermore, these data frame several questions that must be addressed moving forward.

First, how should ‘prolonged’ ICU length of stay, as a surrogate for CCI, be defined? A variety of definitions have been suggested[16]; however, our three-level categorization closely mirrored the cut points suggested by inflections in our fractional polynomial analysis (two and ten days *vs* two and eight days). Furthermore, this categorization clearly shows that survival diverges substantially between the short and intermediate ICU LOS groups and the prolonged ICU LOS group, highlighting that this relatively small group of patients are a population requiring substantial evaluation in future research and quality improvement initiatives.

From a health system perspective, it must be recognized that care that results in over half of patients experiencing death or significant disability comes at a substantial cost. In Ontario, prolonged ICU LOS patients had one-year health systems costs of almost CAD 100,000 more than short ICU LOS patients. While we cannot provide direct measurements of cost-effectiveness or estimate costs per quality adjusted life year, our findings do suggest that such an analysis is warranted in patients experiencing CCI after cardiac surgery. The other knowledge gap that our data suggest must be addressed is regarding more detailed prognostication for cardiac surgery patients with CCI. Currently available models such as EuroSCORE, which were developed to predict short-term mortality, perform poorly when applied to prediction of prolonged ICU stay mortality (c-statistic 0.71).[25] Risk stratification tools that accurately discriminate between patients who will and won’t survive and recover meaningful function need to be developed. Such tools should consider the important effect modifiers that we identified, which suggest that patient who were lower risk before surgery who required prolonged ICU stay were the most likely to die in the subsequent year. Functional outcomes, disability, and health-related quality of life outcomes in relation to post-cardiac surgery ICU length of stay have been rarely studied.[16] Therefore, high-quality prospective studies of patient-centred outcomes post-cardiac surgery ICU stays are also needed to address the needs of this high-risk population.

Strengths and limitations

Our study should be interpreted within the context of its strengths and limitations. Observational studies using health administrative data are at risk of misclassification and confounding bias. Nevertheless, our main exposure and outcome variables have been validated and are known to be accurate, which decreases the risk of misclassification bias. Furthermore, we are not suggesting a direct causal relationship between ICU LOS and outcome but describe the epidemiology and health resource use associated with ICU LOS adjusted for an extensive set of confounders identified through a three-year look-back period. Nevertheless, without data on the specific indication for surgery, physiologic measures such as cardiac function, and intraoperative data, we acknowledge that unmeasured confounding is present. Our data set included procedures representing over 93% of all cardiac surgeries in Ontario;

therefore, we would expect our findings to generalize to patients in Ontario and possibly to jurisdictions with similar demographics and health systems. Nevertheless, the generalizability to other types of cardiac surgery (such as transplantation, ventricular assist devices, and aortic surgery) or different jurisdictions is unknown.

Conclusion

Cardiac surgery patients who require ten days or more of ICU care have increased rates of mortality and loss of independence compared with people who require shorter ICU stays. This relatively small group of patients occupies over 30% of all cardiac surgery ICU bed days, and 55% of these patients will either die prior to hospital discharge or be institutionalized. The associated health system costs are more than CAD 120,000. Accurate risk prediction models are needed to guide appropriate care and decision-making.

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