A derived and validated score to predict prolonged mechanical ventilation in patients undergoing cardiac surgery

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ABSTRACT

Objectives: Prolonged mechanical ventilation after cardiac surgery imposes a significant burden on the patient in terms of morbidity as well as a financial burden on the hospital. We undertook a retrospective analysis of 2 prospectively collected databases developed in tertiary cardiac care centers to derive and validate a risk index predicting prolonged mechanical ventilation after cardiac surgery.

Methods: We studied a retrospective cohort of 32,045 patients undergoing cardiac surgery in 2 hospitals in Toronto, Canada. The development cohort consisted of 21,661 patients at Toronto General Hospital. Data Sunnybrook Health Sciences Centre, Toronto, Canada, with 10,384 patients, served as an institutional validation cohort. We operationally characterized prolonged mechanical ventilation as the duration from surgery completion to extubation exceeding 48 hours.

Results: Prolonged postoperative mechanical ventilation rates in the development and validation cohort were 6% and 7%, respectively. Multivariable regression in the development cohort showed that the following factors were strong predictors of prolonged mechanical ventilation after cardiac surgery: previous cardiac surgery, lower left ventricular ejection fraction, shock, surgery involving repair of congenital heart disease, and cardiopulmonary bypass time. The intraoperative multivariable model retained good discrimination in the validation cohort, achieving a c statistic of 0.787.

Conclusions: Prolonged mechanical ventilation after cardiac surgery can be accurately predicted by readily available pre- and intraoperative information. (J Thorac Cardiovasc Surg 2017;153:108-15)

The total duration of mechanical ventilation model calibration.

Central Message

A risk index derived and validated in 32,045 patients can predict prolonged mechanical ventilation after cardiac surgery.

Perspective

Our study provides a risk index derived in 21,661 patients at Toronto General Hospital, Canada, and validated in 10,384 patients at Sunnybrook Hospital, Canada, to predict prolonged mechanical ventilation after cardiac surgery. The risk index incorporates the use of easily identifiable and routinely recorded pre- and intraoperative variables to predict prolonged mechanical ventilation after cardiac surgery.

See Editorial Commentary page 116.

Despite advances in the perioperative management of cardiac surgical patients, prolonged mechanical ventilation continues to be a significant postoperative problem with a

reported incidence of up to 22% depending on the threshold used to define prolonged mechanical ventilation.¹⁻⁶ Prolonged mechanical ventilation after cardiac surgery imposes a significant burden on the patient in terms of morbidity as well as a financial burden on the hospital.⁷

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
ICU = intensive care unit

Furthermore, the mortality in the group of patients requiring prolonged mechanical ventilation can exceed 40%.⁶ Hence, the development of a reliable prediction model to assist early identification (and treatment) of this problem is paramount.

A risk index that incorporates pre- and intraoperative factors that can accurately predict prolonged mechanical ventilation after cardiac surgery will improve clinical management and decision making in the perioperative milieu. In addition, estimation of risk of prolonged mechanical ventilation could assist in better preoperative counseling and informed decision making. It could also help the intensive care unit (ICU) in allocation of postoperative care resources and provide them with a guide to the estimated length of stay.

To facilitate widespread use, the predictive index should use contemporary perioperative characteristics and easily identifiable risk factors. The dataset used to derive the risk index should be a heterogeneous case mix thus allowing applicability to other centers. More importantly, the derived risk index should be externally validated in another heterogeneous albeit contemporary case mix. Finally, the risk index should be simple, easy to use, and allow a graded estimation of risk of prolonged mechanical ventilation.

Although several studies have identified predictors of prolonged mechanical ventilation after cardiac surgery, these studies are limited by sample size, complex scoring systems, homogeneity of population, and most importantly the lack of a validation cohort separate from model development.^{1-6,8-14}

In view of these limitations, we undertook a retrospective analysis of 2 prospectively collected databases developed in tertiary cardiac care centers to derive and validate a risk index predicting prolonged mechanical ventilation after cardiac surgery.

METHODS

After institutional Research Ethical Board approval, perioperative data on patients undergoing cardiac surgery at Toronto General Hospital (Toronto, Ontario, Canada) and Sunnybrook Health Sciences Centre (Toronto, Ontario, Canada) were retrospectively analyzed from the prospectively collected hospital databases. The derivation and accuracy of these databases have been previously described.¹⁵

Patient Population

All adult patients (age > 18 years) undergoing cardiac surgery with cardiopulmonary bypass (CPB) from January 2000 to April 2012 were included in this study. Patients who did not have a reported duration of mechanical ventilation, those who underwent advanced heart failure therapy, such as ventricular assist device insertion or heart transplantation,

and patients who did not survive until 48 hours after surgery were excluded from this analysis. The cohort at Toronto General Hospital was used as the derivation cohort. Patients at Sunnybrook Health Sciences Centre with similar demographics and exclusion criteria to the derivation cohort formed the validation cohort for this study. The derived risk index was validated on the internal and external cohorts from Toronto General Hospital and Sunnybrook Health Sciences Centre, respectively.

Definition of Outcome Variables

Prolonged mechanical ventilation was defined as duration of postoperative mechanical ventilation exceeding 48 hours. This included patients who had been continuously ventilated for 48 postoperative hours and those who were extubated and subsequently reintubated resulting in a cumulative duration of mechanical ventilation in excess of 48 hours. We also examined total duration of mechanical ventilation, from operation to extubation, as an alternative outcome for prediction.

ICU Management

All patients were admitted to the cardiac ICU after cardiac surgery. Postoperative weaning from mechanical ventilation followed standard institutional protocols at both centers. Patients were considered to be eligible for extubation if they had achieved hemodynamic stability, normothermia (tympanic temperature > 36°C), adequate oxygenation and ventilation indices on arterial blood gas samples, chest drainage of less than 100 mL/hour, normal neurologic findings such as alertness, orientation, and the ability to move all 4 limbs and obey commands on assessment following a decrease in the level of postoperative sedation. The critical care physician in charge of the cardiac surgical ICU was responsible for the final decision to extubate the patient after a successful trial of spontaneous ventilation and confirmation of normal neurologic findings. Similarly, the decision to reintubate the patient was at the discretion of the attending intensivist responsible for the respective cardiac ICU.

Statistical Analysis

Predictor variables were prespecified on the basis of clinical judgement, literature review, and availability in both the development and validation cohorts. To incorporate data from approximately 5% of the patients in the development cohort with missing predictor values, we carried out model development using multiply imputed data via chained equations.¹⁶ Logistic regression analysis was used to construct a prediction model for the binary outcome of prolonged mechanical ventilation outcome; this variable was available in all but 3 patients. For predicting total duration of mechanical ventilation, we considered a stratified Cox model,^{17,18} specific to the reason for extubation; either due to the aforementioned weaning protocol or terminal extubation, operationally defined as extubation occurring within 3 days of death. This approach enables both the prediction of time, rather than postoperative duration exceeding 48 hours, and makes the distinction between these 2 very different reasons for extubation. Model development for each outcome was carried out in 2 stages, with only preoperative characteristics and both pre- and intraoperative information.

Each model was internally validated on 100 bootstrap replications to assess overoptimism in regression coefficients and performance measures. Predictions under each model were performed on patients from the validation cohort with complete data. Model performance was assessed using the c statistic, R-squared value, and calibration curves.¹⁹

RESULTS

Ventilation times were missing for 7 Toronto General Hospital patients. A further 94 (0.4%) patients had unknown postoperative ventilation time. For prolonged mechanical ventilation, all of these cases were excluded

TABLE 1. Development and validation cohorts: patient and surgical characteristics

Variable	Development (N = 21,654)		Validation (N = 10,384)		P value
	N		N		
Age (y)		65 (37-80)		67 (47-81)	<.001
Sex					<.001
Male		15,439 (71.3)		7851 (75.6)	
Female		6215 (28.7)		2533 (24.4)	
Body mass index (kg/m ²)	21,619	27 (21-37)	10,315	27 (21-37)	.91
Emergent surgery	21,651	20,048 (92.6)	10,368	5557 (53.6)	<.001
Year of operation					<.001
2000-2004		10,249 (47.3)		5432 (52.3)	
2005-2008		6219 (28.7)		3070 (29.6)	
2009-2012		5186 (23.9)		1882 (18.1)	
Any previous cardiac surgery		2045 (9.4)		204 (2.0)	<.001
Acute coronary insufficiency	21,638	3231 (14.9)	10,348	3761 (36.3)	<.001
Recent myocardial infarction	21,647	3044 (14.1)		1245 (12.0)	<.001
NYHA classification	20,767		10,320		<.001
Class I		3180 (15.3)		371 (3.6)	
Class II		4345 (20.9)		2928 (28.4)	
Class III		6500 (31.3)		2677 (25.9)	
Class IV		6742 (32.5)		4344 (42.1)	
LVEF (%)	21,613		9441		<.001
40+		18,066 (83.6)		7546 (79.9)	
20-39		3011 (13.9)		1557 (16.5)	
<20		536 (2.5)		338 (3.6)	
Insulin-dependent diabetes mellitus		1305 (6.0)	10,364	622 (6.0)	.94
Medically treated hypertension	21,652	13,065 (60.3)	10,364	6250 (60.3)	.95
Current smoker	21,595	2774 (12.8)	10,363	1571 (15.2)	<.001
Severe COPD	21,653	883 (4.1)	10,360	683 (6.6)	<.001
Previous stroke or TIA	21,647	2009 (9.3)	10,364	775 (7.5)	<.001
PVD or carotid stenosis >70%	21,653	2971 (13.7)	10,362	1290 (12.4)	.002
Creatinine clearance (mL/min)	21,609	81 (38-145)	10,201	81 (38-143)	.134
Preoperative atrial fibrillation		1764 (8.1)		933 (9.0)	.012
CHF	21,653	5089 (23.5)	10,362	1079 (10.4)	<.001
Shock	21,653	322 (1.5)	10,364	74 (0.7)	<.001
Preoperative IABP	21,651	439 (2.0)		222 (2.1)	.53
Valvular disease		8292 (38.3)	10,379	2753 (26.5)	<.001
Total no. of diseased arterial systems			10,383		<.001
0		6737 (31.1)		1885 (18.2)	
1		1317 (6.1)		661 (6.4)	
2		2882 (13.3)		2118 (20.4)	
3		10,718 (49.5)		5719 (55.1)	
Valve surgery		8821 (40.7)		2631 (25.3)	<.001
Repair of congenital defect		1338 (6.2)		83 (0.8)	<.001
Ascending aorta replaced	21,617	2208 (10.2)		587 (5.7)	<.001
CPB time (min)	21,648	95 (52-179)		114 (61-217)	<.001
Circulatory arrest	21,642	856 (4.0)		452 (4.3)	.097
Intraoperative IABP	21,651	416 (1.9)		390 (3.8)	<.001
Prolonged ventilation	21,560	1345 (6.2)	10,330	759 (7.3)	<.001
Total ventilation time (h)		9.25 (4.78-71.12)	10,361	12.67 (7.08-94.40)	<.001
Status at ventilation time					<.001
Censored		94 (0.4)		53 (0.5)	
Extubated		21,212 (98.0)		10,091 (97.2)	
Terminally extubated		348 (1.6)		240 (2.3)	

NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; PVD, peripheral vascular disease; CHF, congestive heart failure; IABP, intra-aortic balloon pump; CPB, cardiopulmonary bypass.

TABLE 2. Multivariable logistic regression model odds ratios for prolonged postoperative mechanical ventilation, at the preoperative and intraoperative stages

Variable	Preoperative		Intraoperative	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Age (y), 55 vs 73	1.28 (0.76-2.17)	.004	1.30 (0.73-2.32)	.36
Sex, female vs male	0.93 (0.82-1.06)	.029	0.97 (0.84-1.11)	.33
Year of operation, 2000-2004 vs 2005-2012	0.94 (0.83-1.06)	<.001	0.96 (0.84-1.09)	.031
Emergent surgery	0.36 (0.29-0.43)	.92	0.45 (0.37-0.55)	.57
Body mass index (kg/m ²), 24 vs 31	1.35 (0.45-4.07)	.28	1.32 (0.46-3.79)	.63
Any previous cardiac surgery	2.17 (1.84-2.57)	<.001	1.31 (1.08-1.58)	<.001
Acute coronary insufficiency	1.18 (0.98-1.43)	.28	1.31 (1.07-1.61)	.50
Recent myocardial infarction	0.98 (0.81-1.18)	<.001	0.99 (0.81-1.21)	.005
NYHA classification, III vs I-II	1.16 (0.97-1.39)	.002	1.08 (0.89-1.30)	.96
NYHA classification, IV vs I-II	1.41 (1.17-1.69)	<.001	1.16 (0.96-1.41)	.017
LVEF (%), 20-39 vs 40+	1.15 (0.98-1.35)	<.001	0.97 (0.82-1.16)	<.001
LVEF (%), <20 vs 40+	2.09 (1.61-2.73)	.171	1.56 (1.17-2.09)	<.001
IDDM	1.14 (0.92-1.42)	.088	1.13 (0.89-1.43)	.010
Medically treated hypertension	1.18 (1.03-1.35)	.84	1.16 (1.01-1.34)	.92
Current smoker	1.08 (0.90-1.29)	.093	1.07 (0.88-1.30)	.44
Severe COPD	1.66 (1.32-2.08)	<.001	1.60 (1.26-2.04)	.132
Previous stroke or TIA	1.19 (1.00-1.42)	.081	1.16 (0.96-1.39)	.77
PVD or carotid stenosis >70%	1.47 (1.26-1.72)	<.001	1.40 (1.19-1.64)	.003
Preoperative atrial fibrillation	1.22 (1.02-1.47)	.020	1.16 (0.95-1.41)	.039
Congestive heart failure	1.66 (1.44-1.93)	.43	1.71 (1.46-1.99)	.48
Shock	1.65 (1.21-2.26)	<.001	1.39 (1.00-1.95)	<.001
Preoperative IABP	2.99 (2.27-3.94)	.046	5.02 (3.76-6.69)	.127
Creatinine clearance (mL/min), 61 vs 104	0.52 (0.15-1.76)	.24	0.53 (0.14-1.93)	.31
Valvular disease	1.81 (1.54-2.12)	<.001	0.71 (0.50-1.01)	<.001
No. of diseased arterial systems, 0 vs 3	1.15 (0.94-1.40)	<.001	0.81 (0.65-1.01)	<.001
Valve surgery			1.21 (0.83-1.77)	.142
Repair of congenital defect			1.33 (1.03-1.72)	<.001
Ascending aorta replaced			1.01 (0.81-1.25)	.053
CPB time (min), 76 vs 120			1.78 (0.68-4.63)	<.001
Circulatory arrest			1.76 (1.36-2.27)	.055
Intraoperative IABP			9.01 (7.11-11.42)	.057

Regression coefficients for age, body mass index, creatinine clearance and bypass time are spline based, but are summarized as a contrast in odds at the first and third sample quartiles. *CI*, Confidence interval; *NYHA*, New York Heart Association; *LVEF*, left ventricular ejection fraction; *IDDM*, insulin-dependent diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *TIA*, transient ischemic attack; *PVD*, peripheral vascular disease; *IABP*, intra-aortic balloon pump; *CPB*, cardiopulmonary bypass.

from model development. The 94 cases were censored when modeling the total duration of mechanical ventilation. Complete predictor and outcome information from Sunnybrook Health Sciences Centre was available for 89% of patients. This gave development and institutional validation cohorts of up to 21,654 and 9244 patients, respectively. Of these, 1345 (6.2%) and 759 (7.3%) patients experienced prolonged mechanical ventilation, respectively. The distribution of the preselected predictor variables and outcomes for the cohorts are summarized in [Table 1](#).

For the binary outcome of prolonged mechanical ventilation, multivariable logistic regression with multiply imputed data from the development cohort led to the identification of 8 to 10 strong predictors of prolonged ventilation; however, all preselected variables were retained in the model regardless of statistical significance ([Table 2](#)).

Internal validation showed little indication of overfitting, regardless of the outcome under prediction and stage, with the apparent performance measures and calibration curves similar to the corrected values ([Figure 1](#)). As one might expect, both the apparent and institutional performance improved with predictions made at the intraoperative stage, with respective c statistics (area under the receiver operating characteristic curve) of 0.840 and 0.787.

In Cox regression analysis, most of the preselected variables appeared useful in predicting the total duration of mechanical ventilation, particularly for nonterminal extubations ([Tables 3](#) and [4](#)). Duration proved relatively difficult to predict with a high degree of discrimination. However, the Cox regression model performed reasonably well, with apparent and institutional c statistics at the intraoperative stage of 0.695 and 0.697, respectively ([Table 5](#)). All calibration curves showed a strong linear

FIGURE 1. Prolonged postoperative mechanical ventilation model calibration.

trend, particularly among patients more likely to have longer duration (Figure 2).

DISCUSSION

This study provides a derived and validated risk index to predict prolonged mechanical ventilation after cardiac surgery. Our risk index incorporates the use of 12 easily identifiable and routinely recorded pre- and intraoperative variables to predict prolonged mechanical ventilation after cardiac surgery. The principal strength of our risk index lies in the successful external validation of most of the internally derived risk factors to predict prolonged ventilation in cardiac surgical patients.

Prediction of prolonged mechanical ventilation after cardiac surgery has been the focus of other studies, and similar or closely related risk factors have been identified by these studies.¹⁻¹⁴ However, none of these studies have validated their respective risk-prediction models in a large validation cohort.

The prevalence of prolonged mechanical ventilation after cardiac surgery and the morbidity and mortality associated with it differs with the threshold used to define prolonged mechanical ventilation.¹⁻¹⁴ The prevalence of prolonged mechanical ventilation in our study of 6.2% and of 7.3% in the derivation and external validation cohorts, respectively, is in agreement with other reports. We chose a threshold of 48 hours to define prolonged mechanical ventilation for several reasons. The Society of Thoracic Surgeons identifies prolonged mechanical ventilation as a total duration of mechanical ventilation >24 hours after exit from the operating room in patients undergoing

isolated coronary artery bypass grafting only.²⁰ The risk profile of cardiac surgical patients has changed over the past decades, with a higher proportion of elderly patients having multiple comorbidities being referred for more complex cardiac surgical procedures.¹⁰ Such patients may not be ideally suited for early extubation and our 48-hour cutoff allows for integration of this subpopulation in the analysis. The 48-hour threshold also helps us to overcome factors such as slow recovery from sedation, transient or minor complications, logistical issues such as staffing, and adherence to local extubation policies and protocols, which could contribute to prolonged mechanical ventilation. Furthermore, we believe that, due to the complexity of cases performed at our hospitals, a 24-hour threshold to define prolonged mechanical ventilation would overestimate the prevalence of this complication.²¹⁻²⁵

That said, the selection of any threshold is somewhat arbitrary and makes no distinction between extubation due to protocol weaning and terminal extubation. Our results show that the same pre- and intraoperative characteristics are also able to reasonably predict the total duration of mechanical ventilation, regardless of the subsequent reason for extubation.

Our analysis consistently identified previous cardiac surgery, cardiogenic shock, and prolonged CPB time as the major predictors of prolonged mechanical ventilation in both the derivation and validation cohorts. The deleterious effects of prolonged CPB are multiple and include the potential of inducing cardiac dysfunction, initiation of a systemic inflammatory response thus leading to activation of mediators, and alteration of normal physiologic homeostasis, which leads to increased capillary permeability including pulmonary circulation. Disruption of the normal endothelial barrier in the pulmonary circulation results in extravasation of lung water, thereby inducing a mild pulmonary edema, which may in turn contribute to respiratory failure and prolonged mechanical ventilation after cardiac surgery.²⁶

The preoperative presence of an intraoperative balloon pump implies critical coronary vascular disease needing emergent cardiac surgical intervention. This setting offers limited opportunity for preoperative optimization and may be responsible for the higher morbidity of prolonged mechanical ventilation as shown in our study. Finally, patients with chronic renal failure have other associated comorbidities, such as peripheral vascular disease, atherosclerosis, diabetes, and hypertension, which contribute to a greater systemic burden of cardiac surgery.

There are multiple implications of the findings presented in our study. They are significant for both clinical management and future research on respiratory complications in cardiac surgical patients. Potentially, they can lead to several changes in the perioperative management of cardiac surgical patients such as better preoptimization

TABLE 3. Multivariable Cox regression model hazard ratios for total duration of mechanical ventilation at the preoperative stage

Variable	Nonterminal extubation		Terminal extubation	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age (y), linear	0.99 (0.99-1.00)	<.001	1.00 (0.99-1.01)	.98
Age (y), nonlinear		<.001		<.001
Sex	0.94 (0.91-0.98)	.001	1.40 (1.11-1.77)	.005
Year of operation	1.28 (1.24-1.32)	<.001	1.36 (1.08-1.71)	.009
Emergent surgery	1.55 (1.45-1.65)	<.001	0.67 (0.48-0.94)	.020
Body mass index (kg/m ²), linear	0.99 (0.98-0.99)	<.001	1.01 (0.98-1.03)	.61
Body mass index (kg/m ²), nonlinear		<.001		.44
Any previous cardiac surgery	0.58 (0.55-0.61)	<.001	1.86 (1.35-2.57)	<.001
Acute coronary insufficiency	0.98 (0.93-1.02)	.32	1.11 (0.79-1.55)	.56
Recent myocardial infarction	1.03 (0.98-1.08)	.27	0.91 (0.64-1.29)	.60
NYHA classification, III vs I-II	0.91 (0.87-0.94)	<.001	1.65 (1.09-2.49)	.018
NYHA classification, IV vs I-II	0.83 (0.80-0.87)	<.001	2.14 (1.41-3.24)	<.001
LVEF (%), 20-39 vs 40+	0.88 (0.85-0.92)	<.001	1.35 (1.01-1.79)	.043
LVEF (%), <20 vs 40+	0.66 (0.61-0.72)	<.001	2.57 (1.72-3.85)	<.001
IDDM	0.87 (0.82-0.93)	<.001	0.96 (0.65-1.41)	.83
Medically treated hypertension	0.94 (0.91-0.97)	<.001	1.08 (0.84-1.40)	.55
Current smoker	0.95 (0.91-0.99)	.022	1.22 (0.88-1.70)	.24
Severe COPD	0.82 (0.76-0.89)	<.001	1.09 (0.72-1.66)	.68
Previous stroke or TIA	0.91 (0.87-0.96)	<.001	1.10 (0.80-1.51)	.55
PVD or carotid stenosis >70%	0.88 (0.85-0.92)	<.001	1.36 (1.02-1.81)	.035
Preoperative atrial fibrillation	0.88 (0.83-0.92)	<.001	1.00 (0.71-1.39)	.98
CHF	0.89 (0.86-0.93)	<.001	1.14 (0.85-1.52)	.37
Shock	0.72 (0.64-0.81)	<.001	1.19 (0.78-1.82)	.42
Preoperative IABP	0.60 (0.55-0.66)	<.001	0.71 (0.45-1.10)	.126
Creatinine clearance (mL/min), linear	1.00 (1.00-1.01)	<.001	0.99 (0.98-1.00)	.012
Creatinine clearance (mL/min), nonlinear		<.001		<.001
Valvular disease	0.73 (0.70-0.76)	<.001	0.93 (0.69-1.25)	.61
No. of diseased arterial systems	0.93 (0.91-0.94)	<.001	0.94 (0.83-1.06)	.28

Regression coefficients for age, body mass index, creatinine clearance and bypass time are spline based, but are summarized as linear and overall linear terms. *CI*, Confidence interval; *NYHA*, New York Heart Association; *LVEF*, left ventricular ejection fraction; *IDDM*, insulin-dependent diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *TIA*, transient ischemic attack; *PVD*, peripheral vascular disease; *CHF*, congestive heart failure; *IABP*, intra-aortic balloon pump.

of patients with high New York Heart Association scores, prediction of ICU workload and subsequent cost incurred by the hospital, the ability to rationalize and tailor postoperative mechanical ventilation strategy for high-risk patients, and finally better preoperative discussion and consent making about the deemed risk and benefit of the proposed surgical procedure. Clinicians and researchers need to be aware that the risk index does not provide absolute risk values for prolonged mechanical ventilation. However, estimation of absolute risk is infrequent and most clinicians prefer to classify patients as low, intermediate, and high risk to simplify the risk stratification process.

Our study has several limitations. Similar to other retrospective observational studies and risk-prediction models, some conclusions of this study may be limited in their application and risk models can only apply variables that have been collected. There is no consensus on the accepted definition of prolonged mechanical ventilation after cardiac surgery, while other investigators have

used a wide range of time frames within a range of 8 hours to 14 days to define prolonged mechanical ventilation following cardiac surgery. Three risk factors in the derivation model failed to achieve statistical significance in the external validation model, and the possible reasons for this have been outlined earlier. Our study was not designed to establish an association between prolonged mechanical ventilation and postoperative outcomes such as long-term survival, mortality, and in-hospital morbidity because others have already studied these complications. We do not have detailed data on the perioperative use of inotropic and vasoactive agents because the use of these agents is predominantly protocolized and institution specific and may confound the results.

In summary, we have described a derived and validated risk index to predict prolonged mechanical ventilation after cardiac surgery using pre- and intraoperative variables that may be routinely collected in most cardiac surgical centers. The heterogeneity of

TABLE 4. Multivariable Cox regression model hazard ratios for total duration of mechanical ventilation at the intraoperative stage

Variable	Nonterminal extubation		Terminal extubation	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age (y), linear	0.99 (0.99-0.99)	<.001	1.01 (0.99-1.02)	.31
Age (y), nonlinear		<.001		<.001
Sex	0.92 (0.89-0.96)	<.001	1.48 (1.16-1.89)	.002
Year of operation	1.31 (1.27-1.35)	<.001	1.33 (1.05-1.69)	.018
Emergent surgery	1.40 (1.31-1.50)	<.001	0.72 (0.52-0.99)	.045
Body mass index (kg/m ²), linear	0.99 (0.99-1.00)	<.001	1.01 (0.99-1.03)	.54
Body mass index (kg/m ²), nonlinear		<.001		.005
Any previous cardiac surgery	0.77 (0.73-0.82)	<.001	1.52 (1.08-2.13)	.016
Acute coronary insufficiency	0.91 (0.87-0.96)	.001	1.14 (0.80-1.63)	.47
Recent myocardial infarction	1.03 (0.98-1.08)	.28	0.94 (0.66-1.35)	.76
NYHA classification, III vs I-II	0.94 (0.90-0.98)	.002	1.45 (0.95-2.23)	.086
NYHA classification, IV vs I-II	0.88 (0.84-0.92)	<.001	1.90 (1.24-2.90)	.003
LVEF (%), 20-39 vs 40+	0.92 (0.88-0.96)	<.001	1.33 (0.98-1.80)	.071
LVEF (%), <20 vs 40+	0.74 (0.67-0.82)	<.001	2.77 (1.84-4.16)	<.001
IDDM	0.87 (0.81-0.93)	<.001	1.01 (0.68-1.51)	.96
Medically treated hypertension	0.95 (0.91-0.98)	.001	1.15 (0.88-1.51)	.31
Current smoker	0.94 (0.90-0.99)	.016	1.29 (0.90-1.84)	.164
Severe COPD	0.84 (0.77-0.91)	<.001	1.09 (0.71-1.68)	.69
Previous stroke or TIA	0.93 (0.88-0.98)	.011	1.07 (0.78-1.47)	.68
PVD or carotid stenosis >70%	0.89 (0.85-0.93)	<.001	1.36 (1.02-1.81)	.037
Preoperative atrial fibrillation	0.91 (0.86-0.96)	<.001	0.85 (0.60-1.21)	.36
CHF	0.88 (0.85-0.92)	<.001	1.12 (0.84-1.48)	.45
Shock	0.79 (0.70-0.89)	<.001	0.96 (0.62-1.48)	.84
Preoperative IABP	0.48 (0.44-0.53)	<.001	1.11 (0.70-1.75)	.66
Creatinine clearance (mL/min), linear	1.01 (1.01-1.01)	<.001	0.99 (0.99-1.00)	.002
Creatinine clearance (mL/min), nonlinear		<.001		<.001
Valvular disease	1.13 (1.00-1.28)	.059	0.54 (0.32-0.91)	.021
No. of diseased arterial systems	0.98 (0.96-1.00)	.047	0.88 (0.77-1.00)	.056
Valve surgery	0.92 (0.81-1.05)	.23	1.22 (0.69-2.16)	.49
Repair of congenital defect	0.88 (0.81-0.95)	.001	0.79 (0.48-1.29)	.34
Ascending aorta replaced	0.96 (0.90-1.02)	.173	0.82 (0.54-1.25)	.36
CPB time (min), linear	0.99 (0.99-0.99)	<.001	1.01 (1.00-1.01)	.017
CPB time (min), nonlinear		<.001		<.001
Circulatory arrest	0.74 (0.68-0.80)	<.001	1.55 (1.02-2.36)	.042
Intraoperative IABP	0.36 (0.33-0.39)	<.001	2.04 (1.45-2.86)	<.001

Regression coefficients for age, body mass index, creatinine clearance and bypass time are spline based, but are summarized as linear and overall linear terms. *CI*, Confidence interval; *NYHA*, New York Heart Association; *LVEF*, left ventricular ejection fraction; *IDDM*, insulin-dependent diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *TIA*, transient ischemic attack; *PVD*, peripheral vascular disease; *CHF*, congestive heart failure; *IABP*, intra-aortic balloon pump; *CPB*, cardiopulmonary bypass.

the patient population and the successful validation of most variables in an external cohort of cardiac surgical patients lend further credibility to our risk index. This risk index may help in preoperative optimization, risk stratification, consent and decision making, and

postoperative financial and resource management in cardiac surgical patients. Further studies may wish to explore the impact of this or other similar risk indices on the perioperative medical, resource and cost management in cardiac surgical patients.

TABLE 5. Performance of the prolonged postoperative ventilation and time to extubation models, at the preoperative and intraoperative stages

Model performance metric	Preoperative			Intraoperative		
	Apparent	Internal	Institutional	Apparent	Internal	Institutional
Prolonged ventilation c statistic	0.777	0.771	0.698	0.840	0.835	0.787
R ²	0.171	0.164	0.060	0.276	0.267	0.125
Time to extubation c statistic	0.653	0.652	0.654	0.695	0.694	0.697
R ²	0.148	0.144	0.141	0.247	0.243	0.240

FIGURE 2. Total duration of mechanical ventilation model calibration. The outcome under prediction is duration lasting more than 48 hours.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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