Medicina Intensiva xxx (xxxx) 502536

Contents lists available at ScienceDirect

Medicina Intensiva

journal homepage: http://www.medintensiva.org/en

Original article

Multistate models for predicting organ failure trajectories in the postoperative period of cardiac surgery

Modelos multiestado para la predicción de trayectorias del fracaso orgánico en el postoperatorio de cirugía cardiaca

Alberto Garrido Callén*, Manuel Pérez Torres, Dovami Vasco Castaño, María González Gómez, Ignacio Fernandéz Martín-Caro, Diego Maqueda Lluva, Marta Martín Muñoz, Manuel Pérez Marquéz

Unidad de Cuidados Intensivos, Hospital Universitario Rey Juan Carlos, Móstoles, Madrid, Spain

ARTICLE INFO

Keywords:
Cardiovascular surgical procedures
Postoperative period
Hemodynamics (pathology)
Multiple organ failure
Risk assessment

ABSTRACT

Objective: Developing a multistate model to predict clinical transitions and their associated risk factors during the ICU postoperative period following cardiac surgery (CS).
Design: An observational, single-center, retrospective study from December 2021 to December 2023. 6 predefined transitions were considered: (T1) ICU admission → haemodynamic failure; (T2) admission → ICU discharge; (T3) haemodynamic failure → second organ failure; (T4) haemodynamic failure → ICU discharge; (T5) second organ failure → ICU discharge; and (T6) second organ failure → death.
Setting: Postoperative period following CS.
Patients: Adults undergoing surgery with cardiopulmonary bypass, excluding immediate postoperative mechanical circulatory support, prior cardiopulmonary arrest, minimally invasive surgery, or reintervention outside the index hospitalization.
Main variables of interest: Comorbidity, functional status, type of intervention, surgical characteristics, and pre- and postoperative haemodynamic status.
Results: n = 197. The final model achieved a C-index = 0.63 (95% CI: 0.58–0.66). The following transition specific adjusted hazard ratios (95% CI) were obtained: in T1, urgent surgery 3.02 (1.85–4.93), age 1.02 (1.00 1.04), central venous pressure at admission 1.05 (1.00–1.10), and shock index (SI) at admission 4.11 (1.56 10.86); in T2, change in left ventricular ejection fraction 0.03 (0.00–0.27) and age 0.98 (0.97–1.00); in T3, aortic cross-clamp time 1.01 (1.00–1.01), number of defibrillations 1.27 (1.01–1.59), mean arterial pressure (MAP) at admission 0.96 (0.93–0.99), and urgent surgery 3.10 (1.19–8.10); in T4, Vasoactive-Inotropic Score at admission 0.97 (0.95–1.00), red blood cell units 0.53 (0.37–0.77), and improvement in right ventricular systolic function 1.61 (1.08–2.38); in T5, previous CS 0.30 (0.11–0.78), SI 0.06 (0.01–0.47), smoker 0.29 (0.13–0.62), and urgent surgery 0.06 (0.01–0.29); and in T6, MAP 0.91 (0.85–0.97) and red blood cell units 1.35 (1.04–1.75).
Conclusions: Multiple risk factors were identified using a multistate model with moderate discrimination for the postoperative period of CS, allowing for the incorporation of the temporal sequence and interdependence of organ failures.

Palabras clave:
Cirugía cardiovascular
Período postoperatorio
Hemodinámica (patología)
Fallo orgánico múltiple
Evaluación del riesgo

RESUMEN

Objetivo: Desarrollar un modelo predictivo multiestado para el postoperatorio de cirugía cardiaca (CCV) en la UCI, identificando factores asociados a cada transición clínica.
Diseño: Estudio observacional, unicéntrico y retrospectivo de diciembre 2021 / diciembre 2023. Se consideraron 6 transiciones predefinidas: (T1) ingreso → fallo hemodinámico; (T2) ingreso → alta de la UCI; (T3) fallo hemo dinámico → segundo fallo orgánico; (T4) fallo hemodinámico → alta de la UCI; (T5) segundo fallo → alta de la UCI; (T6) segundo fallo → fallecimiento.

DOI of original article: https://doi.org/10.1016/j.medin.2026.502536
* Corresponding author.
E-mail address: alberto.garrido@hospitalreyjuancarlos.es (A. Garrido Callén).

https://doi.org/10.1016/j.medine.2026.502536
Received 26 August 2025; Accepted 2 April 2026
Available online xxx
0210-5691/© 2026 Elsevier España, S.L.U. and SEMICYUC. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Please cite this article as: A. Garrido Callén, M. Pérez Torres, D. Vasco Castaño et al., Multistate models for predicting organ failure trajectories in the postoperative period of cardiac surgery, Medicina Intensiva, https://doi.org/10.1016/j.medine.2026.502536

Ámbito: Postoperatorio de CCV.
Pacientes: Adultos intervenidos con circulación extracorpórea excluyéndose: asistencia mecánica inmediata postquirúrgica, parada cardiorrespiratoria previa, cirugía mínimamente invasiva o reintervención fuera de la hospitalización.
Variables de interés principales: Comorbilidad, situación funcional, tipo de intervención, características y situación hemodinámica pre-posquirúrgica.
Resultados: n = 197. El modelo final obtuvo un C-index = 0,63 IC 95% (0,58–0,66). Se obtuvieron los siguientes hazard ratios ajustados por transición con IC 95%: en T1, cirugía urgente 3,02 (1,85–4,93), edad 1,02 (1,00–1,04), presión venosa central al ingreso 1,05 (1,00–1,10) e índice de shock (IS) al ingreso 4,11 (1,56–10,86); en T2, cambio en la fracción de eyección del ventrículo izquierdo 0,03 (0,00–0,27) y edad 0,98 (0,97–1,00); en T3, tiempo de clampaje aórtico 1,01 (1,00–1,01), número de desfibrilaciones 1,27 (1,01–1,59), presión arterial media (PAM) al ingreso 0,96 (0,93–0,99) y cirugía urgente 3,10 (1,19–8,10); en T4, *vasoactive-inotropic score* al ingreso 0,97 (0,95–1,00), concentrado de hematíes 0,53 (0,37–0,77) y mejoría de la función sistólica del ventrículo derecho 1,61 (1,08–2,38); en T5, CCV previa 0,30 (0,11–0,78), IS 0,06 (0,01–0,47), fumador 0,29 (0,13–0,62) y cirugía urgente 0,06 (0,01–0,29); y en T6, PAM 0,91 (0,85–0,97) y concentrado de hematíes 1,35 (1,04–1,75).
Conclusiones: Se identificaron múltiples factores de riesgo mediante un modelo multiestado con discriminación moderada para el postoperatorio de CCV, lo que permitió incorporar la secuencia temporal y la interdependencia de los fallos orgánicos.

Introduction

The management of patients after cardiac surgery (CS) with cardiopulmonary bypass (CPB) presents significant challenges. During the immediate postoperative period, multiple organ dysfunctions may develop, which critically determine prognosis. In this context, stratification of organ failure is usually based on widely used standardized indices such as the Sequential Organ Failure Assessment (SOFA), which allow quantification of severity and estimation of the risk of progression.[1] From this conceptual framework, the postoperative period can be interpreted as a dynamic process characterized by the onset and evolution of interrelated organ dysfunctions.

Circulatory failure is one of the most relevant, early, and frequent complications following CPB withdrawal and may result from different pathophysiological mechanisms: bleeding and hemorrhagic shock, obstructive shock, vasoplegic syndrome, or low cardiac output, potentially progressing to post-cardiotomy cardiogenic shock, its most severe clinical sign and associated with the worst prognosis.[2] The need for vasopressor support and the presence of tissue hypoperfusion align with the cardiovascular component of SOFA as markers of significant hemodynamic dysfunction.[3] Acute kidney injury (AKI), particularly when progressing to stage ≥ II according to KDIGO 2012 criteria, is consistently associated with increased morbidity and mortality.[4,5] Respiratory dysfunction is assessed using the PaO2/FiO2 ratio, included in SOFA, with a threshold < 200 mmHg proposed in cardiac surgery as a marker of worse outcomes.[6] Similarly, hepatic dysfunction may develop, with total bilirubin values > 3 mg/dL or > 6 mg/dL considered clinically relevant cut-off points.[7,8] Finally, within the hematological component of SOFA, postoperative thrombocytopenia lacks universally established thresholds, with commonly used cut-offs of < 50,000 or < 75,000 platelets/μL depending on the literature consulted.[9,10]

The main limitation lies in the fact that classical models applied to the postoperative period of cardiac surgery provide an essentially static estimation of risk, based on baseline variables and focused on final outcomes such as in-hospital mortality, without incorporating subsequent clinical progression or the occurrence of intermediate complications.[11,12] In a scenario characterized by dynamic interaction between multiple organ dysfunctions, there is a need for tools capable of integrating the temporal sequence of events and their mutual influence. Although severity indices exist to categorize multiorgan failure, they do not explicitly model progression between clinical states nor the competition between alternative outcomes.[13–15] In contrast, multistate models allow the postoperative period to be represented as a dynamic process composed of successive transitions between intermediate states—namely organ failures—explicitly incorporating temporal dependency and the competitive nature of events. This approach facilitates identification of factors associated with each specific transition and provides an evolutionary prognostic estimation, more closely aligned with the real clinical trajectory of patient management during the ICU stay.

Patients and methods

Design

We conducted a single-center, retrospective, observational study including patients undergoing cardiac surgery from December 2021 through December 2023 in the general ICU of *Hospital Universitario Rey Juan Carlos* (Móstoles, Spain). Data collection and protocol were approved by the local ethics and research committee (June 11th, 2024; record No. 11/24).

Inclusion criteria

Surgery requiring CPB during the study period.

Exclusion criteria

Age < 18 years, preoperative cardiac arrest, inability to wean from CPB requiring immediate extracorporeal support (< 24 h), minimally invasive surgery, or cardiac reintervention outside the index hospitalization during the study period.

Methodology

Variables related to comorbidity and hemodynamic status were extracted, including baseline preoperative parameters and those recorded at ICU admission. Intraoperative anesthetic management was homogeneous according to current clinical practice, and postoperatively all patients were admitted under invasive mechanical ventilation with intravenous sedoanalgesia.[16,17] Time-to-event variables and their censoring were recorded:

- ICU admission.
- Hemodynamic failure: baseline norepinephrine ≥0.2 mcg/kg/min or lactate > 3 mmol/L or base excess < −5 mEq/L.
- Second organ failure occurring first: PaO2/FiO2 < 200, platelets < 50,000/μL, bilirubin > 6 mg/dL, or AKI KDIGO stage II.[18]
- ICU discharge.
- All-cause mortality.

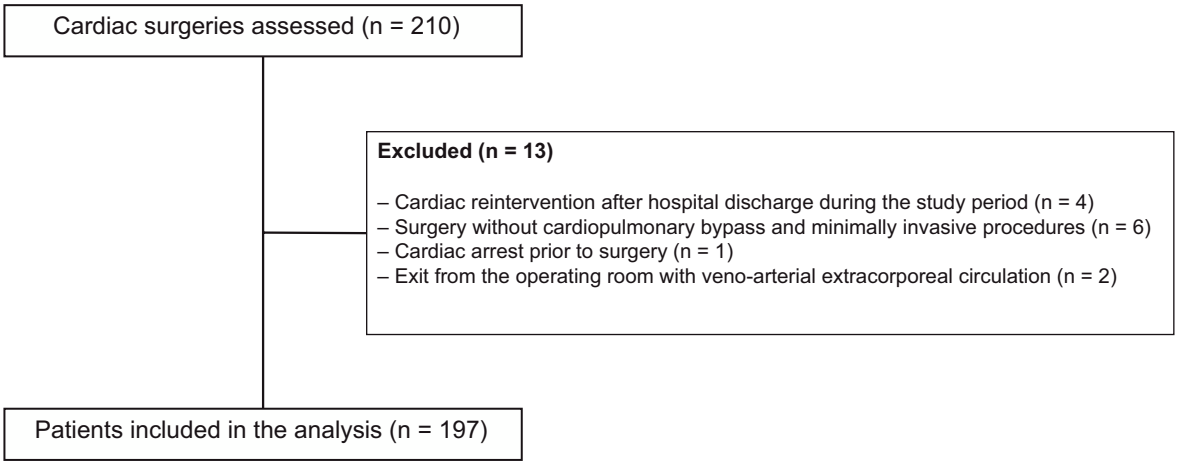

Fig. 1. Flowchart of patient screening, exclusions, reasons, and final analyzed cohort.

Table 1
Description of comorbidities, type of surgery, and outcomes of the total analyzed cohort.

Variables (N = 197)[1]			
Comorbidity		Surgical	
Male sex	132 (67%)	Elective surgery	182 (92%)
Age (years)	67 (60–73)	Type of operation according to EuroSCORE II	54 (27%)
BMI (kg/m^2)	27.5 (24.3–30.4)	• Coronary revascularization only	54 (27%)
Hypertension	136 (69%)	• Major surgery without revascularization	101 (52%)
Dyslipidemia	118 (60%)	• 2 major procedures	36 (18%)
Smoking	39 (20%)	• ≥3 major procedures	6 (3.0%)
Diabetes mellitus	53 (28%)	Endocarditis	17 (8.6%)
Ischemic heart disease	45 (33%)	Any valvular intervention	127 (65%)
Previous cardiac surgery	15 (7.6%)	Any coronary revascularization	69 (35%)
Atrial fibrillation/flutter	49 (25%)	Thoracic aorta surgery	27 (14%)
NYHA > 2	21 (10.5%)	Central cannulation	185 (94%)
Chronic kidney disease	126 (64%)	Direct cardioplegia administration	117 (60%)
Charlson index	2 (1–3)	Combined cardioplegia administration	70 (36%)
Functional class (CFS)	2 (1–2)	Blood cardioplegia	91 (46%)
Predicted mortality (EuroSCORE II, %)	3.2 (2.1–6.9)	Hypothermia at admission (°C)	34 (33–35)
Pump time (min)	105 (90–132)	Aortic cross-clamp time (min)	76 (61–96)

Outcomes of interest			
ICU readmission during the length of stay	16 (8.12%)	Time to extubation (hours)	5.05 (3.15–9.15)
Sternal reopening	16 (8.12%)	Percutaneous tracheostomy	7 (3.35%)
Length of the ICU stay (hours)	53.2 (45.6–82.8)	Hospital length of stay (hours)	166 (134–232)
Renal replacement therapy	14 (7.10%)	Refractory shock (norepinephrine >0.5 mcg/kg/min)	20 (10.15%)
Extracorporeal circulation for refractory cardiogenic shock (>24 h after CPB)	3 (1.5%)	Mortality	13 (6.6%)

Values are expressed as median (IQR) or n (%).
BMI: body mass index; NYHA: New York Heart Association; CFS: Clinical Frailty Score; ICU: intensive care unit.

Quantitative variables were expressed as median and interquartile range (IQR, P25–P75), and qualitative variables as number and percentage. A homogeneous-time Markov model with an acyclic structure was predefined. Univariate analysis was performed followed by a multivariate predictive analysis using proportional hazards stratified by transition.[19] A $P < .05$ was considered statistically significant (see Patients and Methods in them supplementary data).

Results

After the exclusion of 13 patients, a total of 197 were finally analyzed (Fig. 1). Table 1 describes the comorbidities, types of surgery, and outcomes of the cohort. Of all ICU patients, 111 (56.35%) developed hemodynamic failure and 86 (43.65%) were discharged from the ICU. Among those who developed hemodynamic failure, 60 (54.05%) pro-

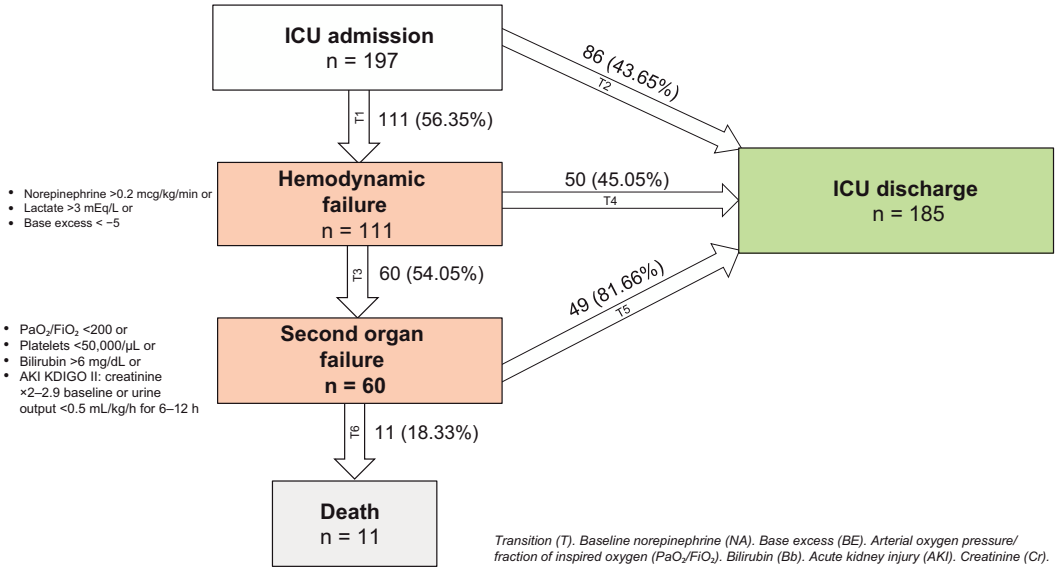

Fig. 2. Definition of clinical states with number of patients per transition and percentage relative to total n (%).

Table 2
Evolution of estimated point probabilities with 95%CI of being in a specific state according to time elapsed since admission and the initial state (rows), using the Delta method.

	State	2 h	12 h	24 h	48 h	96 h
From the ICU	ICU	0.79 (0.72–0.85)	0.68 (0.60–0.75)	0.57 (0.49–0.65)	0.35 (0.28–0.43)	0.08 (0.04–0.12)
	Hemodynamic failure	0.21 (0.14–0.27)	0.24 (0.18–0.31)	0.23 (0.17–0.29)	0.15 (0.10–0.20)	0.05 (0.02–0.08)
	Second organ failure	0.01 (0.00–0.01)	0.08 (0.04–0.11)	0.13 (0.09–0.18)	0.15 (0.10–0.19)	0.10 (0.06–0.13)
	ICU discharge	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.06 (0.02–0.09)	0.34 (0.27–0.41)	0.76 (0.70–0.82)
	Death	0.00 (0.00–0.00)	0.00 (0.00–0.01)	0.01 (0.00–0.02)	0.01 (0.00–0.02)	0.01 (0.00–0.03)
From hemodynamic failure	Hemodynamic failure	0.95 (0.89–1.00)	0.67 (0.57–0.77)	0.48 (0.38–0.58)	0.26 (0.18–0.34)	0.09 (0.04–0.13)
	Second organ failure	0.05 (0.00–0.11)	0.32 (0.22–0.42)	0.44 (0.34–0.54)	0.41 (0.32–0.51)	0.26 (0.18–0.35)
	ICU discharge	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.04 (0.01–0.08)	0.29 (0.21–0.38)	0.60 (0.51–0.69)
	Death	0.00 (0.00–0.00)	0.01 (0.00–0.04)	0.04 (0.00–0.08)	0.04 (0.00–0.08)	0.05 (0.00–0.09)
From second organ failure	Second organ failure	1.00 (1.00–1.00)	0.96 (0.88–1.00)	0.89 (0.78–1.00)	0.67 (0.54–0.80)	0.41 (0.28–0.53)
	ICU discharge	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.22 (0.12–0.33)	0.47 (0.34–0.60)
	Death	0.00 (0.00–0.00)	0.04 (0.00–0.12)	0.11 (0.00–0.22)	0.11 (0.00–0.22)	0.12 (0.01–0.24

Initial state: intensive care unit (ICU). Hemodynamic failure state (HEMODYNAMIC FAILURE). Second organ failure state (SECOND ORGAN FAILURE). Absorbing state: discharge to hospital ward (ICU DISCHARGE). Absorbing state: death from all causes (DEATH).

gressed to a second organ failure and 50 (45.05%) were discharged. Of those with a second failure, 49 (81.66%) were discharged from the ICU and 11 (18.33%) died. Within this framework, all deaths occurred after passing through the second failure state, with no sudden deaths recorded from any other state (Fig. 2).

Table 2 and its graphical representation in Fig. 3 show the cumulative transition risk starting from the three non-absorbing states.

In the final multivariate model stratified by transitions with proportional hazards and homogeneous time, a concordance index of 0.63 (95%CI, 0.58–0.69) was obtained as a measure of overall discrimination, with results shown in Table 3.

From ICU admission, the risk of hemodynamic failure (transition 1) was higher in patients undergoing urgent surgery, with an HR, 3.02 (1.82–4.93), increasing by 2.2% per additional year of age (HR, 1.02 [1.00–1.04]). Likewise, each unit increase in the shock index (SI) at admission was associated with an increased risk (HR, 4.12 [1.56–10.86]). These effects were adjusted for central venous pressure (CVP) at admission (HR, 1.05 [1.00–1.10]), which, although not reaching statistical significance, was retained as a confounding variable and structural adjustment factor in the model.

In patients without hemodynamic failure, the probability of ICU discharge (transition 2) decreased with each percentage point worsening in left ventricular ejection fraction (LVEF) (HR, 0.03 [0.00–0.27]). Age was also negatively associated with ICU discharge probability (HR, 0.98 [0.97–1.00]).

Among patients who developed hemodynamic failure, progression to multiorgan dysfunction (transition 3) was associated with a 0.8% increase in risk per additional minute of aortic cross-clamp time (HR, 1.01 [1.00–1.02]). Each defibrillation after CPB increased the risk (HR, 1.27 [1.01–1.59]), while mean arterial pressure (MAP) at admission acted as a protective factor (HR, 0.96 [0.93–0.99]). Emergency surgery was associated with an HR, 3.11 (1.19–8.10). From this state, the hazard of ICU discharge (transition 4) decreased with higher values of the Vasoactive-Inotropic Score[20] (VIS) (HR, 0.98 [0.95–0.99]), with a greater number of packed red blood cell transfusions (HR, 0.53 [0.37–0.77]), and increased with each improvement in right ventricular systolic function category after CPB (HR, 1.61 [1.09–2.38]).

In patients who reached the second failure, the risk of all-cause mortality (transition 6) was determined by MAP, with higher values acting as a protective factor (HR, 0.91 [0.85–0.97]), and by each transfused packed red blood cell unit (HR, 1.35 [1.04–1.75]). From the second failure state, the risk of ICU discharge (transition 5) was lower in patients with previous cardiac surgery (HR, 0.30 [0.11–0.78]), higher shock index (HR, 0.06 [0.007–0.47]), smoking status (HR, 0.29 [0.14–0.62]), or emergency surgery (HR, 0.06 [0.01–0.29]).

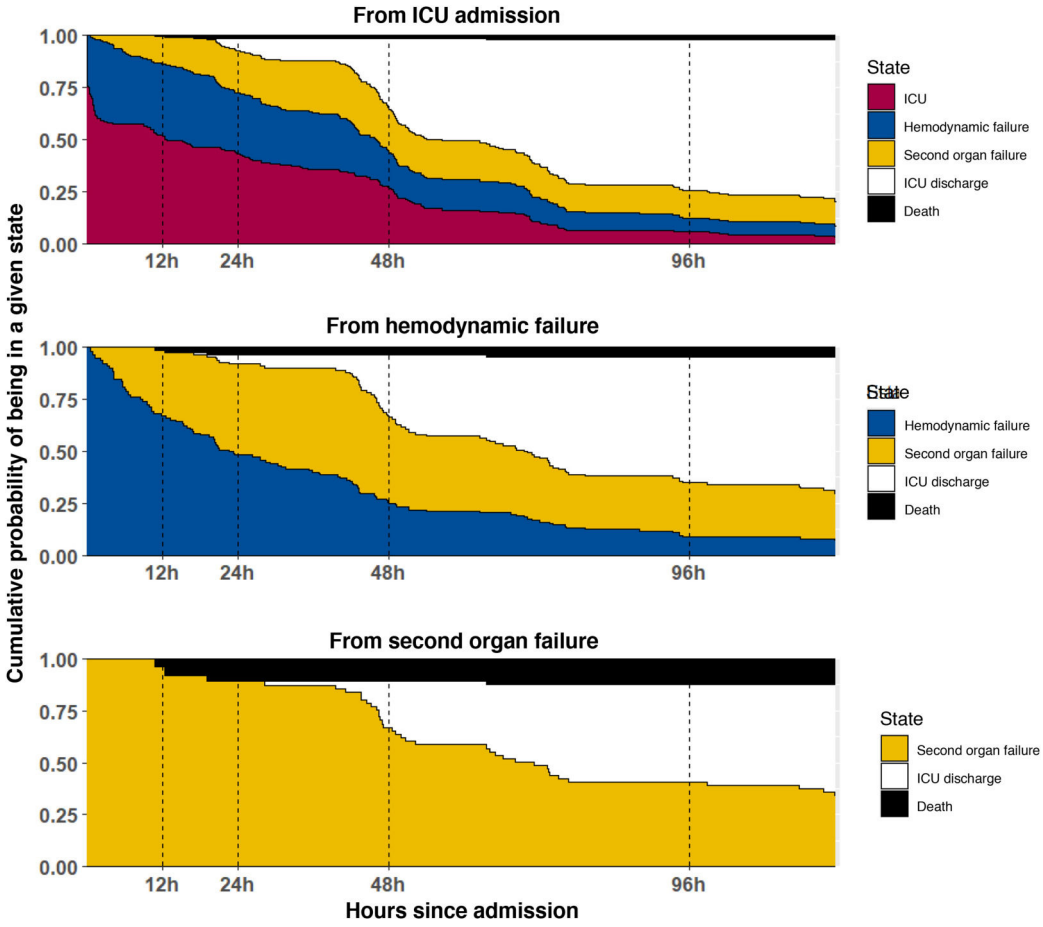

Fig. 3. Probability of state occupancy according to the initial clinical event: from ICU, hemodynamic failure, or second organ failure, without covariates. The vertical axis indicates the cumulative probability of being in each state, while the horizontal axis shows time in hours since admission. Black dashed vertical lines indicate time points of potential interest (12, 24, 48, and 96 h).

Table 3
Final multivariate Cox proportional hazards regression model stratified by transition. Harrell's C concordance index by transition and overall model, with 95%CI estimated by BCa bootstrap (n = 1000 samples).

Transition number	Variables	HR	Lower 95%CI	Upper 95%CI	*P* value
1. ICU → hemodynamic failure	Emergency surgery	3.022	1.852	4.933	< .001
(C-index: 0.65 [0.57–0.70])	Age (years)	1.022	1.003	1.042	.022
	CVP at admission (mmHg)	1.047	0.999	1.096	.052*
	SI at admission	4.115	1.558	10.864	.004
2. ICU → ICU discharge	Change in LVEF pre-admission (%)	0.028	0.003	0.265	.002
(C-index: 0.56 [0.49–0.61])	Age (years)	0.984	0.969	0.999	.036
3. Hemodynamic failure →	Aortic cross-clamp time (min)	1.008	1.001	1.015	.034
second organ failure(C-index:	No. of defibrillations	1.268	1.014	1.586	.036
0.69 [0.56–0.74])	MAP at admission (mmHg)	0.962	0.933	0.992	.014
	Emergency surgery	3.105	1.190	8.101	.020
4. Hemodynamic failure → ICU	VIS at admission	0.975	0.954	0.996	.018
discharge (C-index: 0.70	Packed red blood cells (units)	0.532	0.366	0.774	< .001
[0.59–0.78])	Improvement in RV systolic dysfunction grade	1.607	1.085	2.381	.018
5. Second **organ failure → ICU**	Previous cardiac surgery	0.296	0.113	0.777	.013
discharge (C-index: 0.80	SI at admission	0.057	0.007	0.474	.008
[0.66–0.86])	Smoking	0.290	0.135	0.623	.001
	Emergency surgery	0.057	0.011	0.294	< .001
6. Second **organ failure → death**	MAP at admission (mmHg)	0.909	0.850	0.973	.005
(C-index: 0.89 [0.75–0.95])	Packed red blood cells (units)	1.347	1.039	1.747	.025
Overall model C-index: 0.626 (0.577–0.658)					

Mean arterial pressure (MAP). Central venous pressure (CVP). Right ventricle (RV). Shock index (SI). Intensive care unit (ICU). Preoperative (Pre). Admission (Adm). Bias-corrected and accelerated (BCa).

* *P* > .05, not statistically significant.

Discussion

The results obtained are consistent with clinical practice and aligned with the available scientific evidence, while also being integrated into a dynamic and temporal framework that reflects the real evolution of critically ill patients after cardiac surgery. Beyond identifying isolated risk factors, the model provides added value by enabling analysis of clinical progression as a sequence of transitions between states, estimating conditional risks dependent on the stage of evolution and accounting for the competing nature of outcomes. The model demonstrates the independent relevance of the included covariates, maintaining stable discrimination even after adjustment for potentially confounding variables such as type of intervention, comorbidities, baseline frailty, and preoperative clinical status.

In transition 1, the shock index (SI), as a marker of hemodynamic dysfunction after cardiac surgery, has been associated with hard outcomes in revascularization procedures and pediatric postoperative settings.[21,22] Age as a risk factor shows contradictory findings, being associated with difficult weaning from CPB and post-CPB vasoplegia, while in other series it may be protective or neutral in post-cardiotomy shock.[23–25] The role of CVP may be explained by intraoperative volume management and the relationship between vascular tone and venous return, and therefore the resulting congestion and/or right ventricular dysfunction. Its interpretation remains complex outside the individual clinical context and its interaction with other hemodynamic variables, although broadly speaking, increased CVP appears to be associated with mortality and AKI.[26,27]

In transition 3, ischemia time is closely related to the duration of the surgical procedure and the amount of cardioplegia administered, and therefore to myocardial protection as a determinant of morbidity and mortality, although it is difficult to control due to variability between centers, procedures, and other factors.[28] Regarding defibrillations after CPB withdrawal, malignant reperfusion arrhythmias are a well-known and long-established risk factor associated with myocardial stunning.[29]

In transition 2, an increase in left ventricular ejection fraction (LVEF) has been associated with a shorter time to ICU discharge, consistent with findings from studies on revascularization surgery,[30] aortic valve replacement,[31] and mitral valve replacement,[32] and in our case this effect was independent of the type of procedure. Once again, age was a risk factor for prolonged ICU stay, as previously reported.[33] In transition 4, both the number of intraoperative packed red blood cell units, the Vasoactive-Inotropic Score (VIS), and worsening right ventricular systolic function at admission were factors that delayed ICU discharge, as previously described.[34–36]

Regarding transition 5, late reintervention is a known factor associated with increased morbidity and mortality; in our case, the sample size was insufficient to adjust for the type of prior underlying intervention.[37] Smoking as a risk factor is well established and has recently been associated with a postoperative mortality HR of 1.24 (1.07–1.44).[38] Finally, in transition 6, MAP, as an indirect reflection of possible perioperative bleeding or a pre-shock state, has been identified as a relevant risk factor and is currently under investigation.[39,40] Its isolated interpretation is complex due to the dynamic interaction between cardiac output, vascular resistance, and critical closing pressure, which determine its value and, in such a complex scenario, may reflect a multifactorial condition. The number of transfused packed red blood cell units, as a surrogate for the severity of perioperative bleeding, is a well-studied risk factor for mortality and postoperative complications, although this may be somewhat reductionist given the complexity of hemorrhagic coagulopathy, the degree of heart failure, and perioperative management within *Patient Blood Management* programs.[41]

Nevertheless, it is important to acknowledge methodological limitations, which are largely inherent to the study design. First, certain relevant variables—such as estimated intraoperative bleeding, ultrafiltration rate, MAP during CPB, hemostatic adjuncts, timing of antithrombotic discontinuation, and amount of cardioplegia—could not be collected. In addition, the nature of the postoperative setting implies that each state represents an oversimplification of clinical reality, with an artificial and categorical definition that does not account for the underlying pathophysiological causes of each failure given their heterogeneity; the selected thresholds are therefore open to criticism. Hemodynamic failure is the most paradigmatic example, as it was defined using a macro-hemodynamic criterion such as norepinephrine dose, along with 2 perfusion-related markers, namely base deficit and lactate levels.[42,43] Furthermore, the number of transitions per state—and consequently the sample size—may represent a limitation. Although developing a more complex model, relaxing the Markov property, and incorporating more transitions could provide a more faithful representation of clinical practice, this would likely compromise the statistical power of the analysis. Additionally, no adjustment was made for nonlinear components in quantitative variables to preserve model parsimony and interpretability. Finally, the single-center nature of the study and the specific characteristics of the patient population limit the generalizability of the results, given the predominance of elective procedures in patients with good baseline functional status and predominantly non-complex cardiovascular disease.

Conclusions

This study demonstrates the feasibility of using multistate predictive models based on Cox regression to analyze the risk of transitions between different organ failures in the postoperative period of cardiac surgery. Through this approach, multiple risk factors associated with the development of hemodynamic failure, its progression to a second organ dysfunction, and subsequent outcomes of death or ICU discharge were identified, independently of baseline status, comorbidity, and type of surgery, yielding a predictive model with moderate discrimination.

Authors' contributions

Study design, data collection, analysis, and manuscript writing: Alberto Garrido Callén[ab].

Data collection, manuscript writing, and review: Manuel Pérez Torres[a], Dovami Vasco Castaño[a], and Manuel Pérez Marquéz[a].

Data collection and manuscript review: María González Gómez[a], Ignacio Fernández Martín-Caro[a], Diego Maqueda Lluva[a], and Marta Martín Muñoz[a].

Declaration of Generative AI and AI-assisted technologies in the writing process

Not used.

Funding

None declared.

Declaration of competing interest

None declared.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medine.2026.502536.

References

1. Jiménez Rivera JJ, Llanos Jorge C, López Gude MJ, Pérez Vela JL, en representación del GTCICYRCP. Perioperative management in cardiovascular surgery [Article in English, Spanish]. *Med Intensiva (Engl Ed)*. 2021;45:175–183.

2. Pérez Vela JL, Llanos Jorge C, Duerto Álvarez J, Jiménez Rivera JJ. Clinical management of postcardiotomy shock in adults. *Med Intensiva (Engl Ed)*. 2022;46:312–325.
3. Pérez Vela JL, Martín Benítez JC, Carrasco González M, et al. Grupo de Trabajo de Cuidados Intensivos Cardiológicos y RCP de SEMICYUC, con el aval científico de la SEMICYUC (2012). Clinical practice guide for the management of low cardiac output syndrome in the postoperative period of heart surgery [Article in Spanish]. *Med Intensiva*. 2012;36:e1–e44.
4. Petäjä L, Vaara S, Liuhanen S, et al. Acute kidney injury after cardiac surgery by complete KDIGO criteria predicts increased mortality. *J Cardiothorac Vasc Anesth*. 2017;31:827–836.
5. Howitt SH, Grant SW, Caiado C, et al. The KDIGO acute kidney injury guidelines for cardiac surgery patients in critical care: a validation study. *BMC Nephrol*. 2018;19:149.
6. Esteve F, Lopez-Delgado JC, Javierre C, et al. Evaluation of the PaO2/FiO2 ratio after cardiac surgery as a predictor of outcome during hospital stay. *BMC Anesthesiol*. 2014;14:83.
7. Raveendran D, Penny-Dimri JC, Segal R, et al. The prognostic significance of postoperative hyperbilirubinemia in cardiac surgery: systematic review and meta-analysis. *J Cardiothorac Surg*. 2022;17:129.
8. Farag M, Veres G, Szabó G, Ruhparwar A, Karck M, Arif R. Hyperbilirubinaemia after cardiac surgery: the point of no return. *ESC Heart Fail*. 2019;6:694–700.
9. Griffin BR, Bronsert M, Reece TB, et al. Thrombocytopenia after cardiopulmonary bypass is associated with increased morbidity and mortality. *Ann Thorac Surg*. 2020;110:50–57.
10. Velho TR, Pereira RM, Guerra NC, et al. The impact of cardiopulmonary bypass time on the Sequential Organ Failure Assessment score after cardiac surgery. *Interdiscip Cardiovasc Thorac Surg*. 2024;38:ivae082.
11. O'Brien SM, Feng L, He X, et al. The Society of Thoracic Surgeons 2018 adult cardiac surgery risk models: part 2—statistical methods and results. *Ann Thorac Surg*. 2018;105:1419–1428.
12. Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734–744.
13. Cobert J, Frere Z, Wongsripuemtet P, et al. Trends in the utilization of multiorgan support among adults undergoing high-risk cardiac surgery. *J Cardiothorac Vasc Anesth*. 2024;38:1987–1995.
14. Velho TR, Pereira RM, Paixão T, et al. Sequential Organ Failure Assessment score in the ICU as a predictor of long-term survival after cardiac surgery. *Crit Care Explor*. 2022;4:e0682.
15. Huebner M, Wolkewitz M, Enriquez-Sarano M, Schumacher M. Competing risks need to be considered in survival analysis models for cardiovascular outcomes. *J Thorac Cardiovasc Surg*. 2017;153:1427–1431.
16. Jeppsson A, Rocca B, Hansson EC, et al. 2024 EACTS guidelines on perioperative medication in adult cardiac surgery. *Eur J Cardiothorac Surg*. 2024;67:ezae355.
17. Casselman FPA, Lance MD, Ahmed A, et al. 2024 EACTS/EACTAIC guidelines on patient blood management in adult cardiac surgery in collaboration with EBCP. *Eur J Cardiothorac Surg*. 2025;67:ezae352.
18. Brown JK, Shaw AD, Mythen MG, et al. Adult cardiac surgery-associated acute kidney injury: joint consensus report. *J Cardiothorac Vasc Anesth*. 2023;37:1579–1590.
19. de Wreede LC, Fiocco M, Putter H. The mstate package for estimation and prediction in non- and semi-parametric multi-state and competing risks models. *Comput Methods Programs Biomed*. 2010;99:261–274.
20. Belletti A, Lerose CC, Zangrillo A, Landoni G. Vasoactive-inotropic score: evolution, clinical utility, and pitfalls. *J Cardiothorac Vasc Anesth*. 2021;35:3067–3077.
21. Said A, Salah M, Samir M, Magdy R. Correlation between shock index and postoperative outcomes for patients undergoing on-pump coronary artery bypass graft surgery (an observational study). *Egypt J Anaesth*. 2023;39:722–730.
22. Hagel JA, Sperotto F, Laussen PC, Salvin JW, Bachu A, Kheir JN. Shock index coronary perfusion pressure, and rate pressure product as predictors of adverse outcome after pediatric cardiac surgery. *Pediatr Crit Care Med*. 2021;22:e67–e78.
23. Denault AY, Tardif JC, Mazer CD, et al. Difficult and complex separation from cardiopulmonary bypass in high-risk cardiac surgical patients: a multicenter study. *J Cardiothorac Vasc Anesth*. 2012;26:608–616.
24. Barrera Sánchez M, Royo Villa C, Ruiz de Gopegui P, Gutiérrez Ibañes P, Carrillo López A. Factors associated with vasoplegic shock in the postoperative period of cardiac surgery and influence on morbidity and mortality of the use of arginine vasopressin as rescue therapy. *Med Intensiva (Engl Ed)*. 2024;48:392–402.
25. Soltesz EG, Parks RJ, Jortberg EM, Blackstone EH. Machine learning-derived multivariable predictors of postcardiotomy cardiogenic shock in high-risk cardiac surgery patients. *JTCVS Open*. 2024;22:272–285.
26. Williams JB, Peterson ED, Wojdyla D, et al. Central venous pressure after coronary artery bypass surgery: does it predict postoperative mortality or renal failure? *J Crit Care*. 2014;29:1006–1010.
27. Zhao Y, Zhang H, Wang X, Liu D. Impact of central venous pressure during the first 24 h and its time-course on the lactate levels and clinical outcomes of patients who underwent coronary artery bypass grafting. *Front Cardiovasc Med*. 2023;10:1036285.
28. Santarpino G, Gazdag L, Caprile M. Cross-clamp time and complications: which comes first, the chicken or the egg? *Ann Thorac Surg*. 2017;104:2124.
29. Zhou N, Gong J, Liang X, et al. Preoperative risk prediction score for and in-hospital clinical outcomes of reperfusion ventricular fibrillation after release of aortic cross-clamps: a retrospective study. *J Cardiothorac Vasc Anesth*. 2023;37:127–134.
30. Downey MC, Hooks M, Gravely A, et al. Perioperative changes in left ventricular systolic function following surgical revascularization. *PLoS One*. 2022;17:e0277454.
31. Une D, Mesana L, Chan V, et al. Clinical impact of changes in left ventricular function after aortic valve replacement: analysis from 3112 patients. *Circulation*. 2015;132:741–747.
32. Suri RM, Schaff HV, Dearani JA, et al. Recovery of left ventricular function after surgical correction of mitral regurgitation caused by leaflet prolapse. *J Thorac Cardiovasc Surg*. 2009;137:1071–1076.
33. Veenith T, Sharples L, Gerrard C, Valchanov K, Vuylsteke A. Survival and length of stay following blood transfusion in octogenarians following cardiac surgery. *Anaesthesia*. 2010;65:331–336.
34. Bootsma IT, Scheeren TWL, de Lange F, Haenen J, Boonstra PW, Boerma EC. Impaired right ventricular ejection fraction after cardiac surgery is associated with a complicated ICU stay. *J Intensive Care*. 2018;6:85.
35. Koponen T, Karttunen J, Musialowicz T, Pietiläinen L, Uusaro A, Lahtinen P. Vasoactive-inotropic score and the prediction of morbidity and mortality after cardiac surgery. *Br J Anaesth*. 2019;122:428–436.
36. Wisniewski AM, Wang XQ, Sutherland G, et al. Multi-institutional model to predict intensive care unit length of stay after cardiac surgery. *J Thorac Cardiovasc Surg*. 2025;170:784–792.
37. Bianco V, Kilic A, Gleason TG, et al. Reoperative cardiac surgery is a risk factor for long-term mortality. *Ann Thorac Surg*. 2020;110:1235–1242.
38. Abreu A, Máximo J, Leite-Moreira A. Preoperative smoking status and long-term survival after coronary artery bypass grafting: a competing risk analysis. *Eur J Cardiothorac Surg*. 2024;65:ezae183.
39. McIlroy D, Murphy D, Kasza J, et al. Association of postoperative blood pressure and bleeding after cardiac surgery. *J Thorac Cardiovasc Surg*. 2019;158:1370–1379.
40. Descamps R, Amour J, Besnier E, et al. Perioperative individualized hemodynamic optimization according to baseline mean arterial pressure in cardiac surgery patients: rationale and design of the OPTIPAM randomized trial. *Am Heart J*. 2023;261:10–20.
41. Woldendorp K, Manuel L, Srivastava A, et al. Perioperative transfusion and long-term mortality after cardiac surgery: a meta-analysis. *Gen Thorac Cardiovasc Surg*. 2023;71:323–330.
42. Zante B, Reichenspurner H, Kubik M, et al. Base excess is superior to lactate-levels in prediction of ICU mortality after cardiac surgery. *PLoS One*. 2018;13:e0205309.
43. Algarni KD. The effect of hyperlactatemia timing on the outcomes after cardiac surgery. *Cardiothorac Surg*. 2020;28:18.