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Background: To identify the risk factors for postoperative delirium (POD) after cardiac surgery in frail elderly patients and develop a receiver operating characteristic (ROC) prediction model to confirm the effectiveness.

Methods: This was a prospective observational study, patients were assessed preoperatively according to the frailty index (FI) scale. Cerebral (SctO₂) was assessed at different time points using near-infrared spectroscopy (NIRS). On the basis of the occurrence of POD within 7 days after surgery, patients were divided into POD and non-POD groups. Risk factors were analyzed using logistic regression analysis, while their predictive values were evaluated using the receiver operating characteristic curve analysis.

Results: POD was significantly associated with frailty, lower preoperative MMSE scores, hyperlipidemia, diabetes, cerebrovascular disease, lower hemoglobin level, lower albumin level, longer operation time, longer CPB time, lower SctO₂ at T5, and lower SctO_{2baseline} (P < 0.05). SrtO₂ and SmtO₂ did not differ significantly between groups. FI, preoperative MMSE score, and operation time as independent risk factors (P < 0.05). Significant predictive value was demonstrated in all 3 variables (P < 0.001; respectively). Among them, high sensitivity and specificity were observed with the FI (cut-off value 0.27, sensitivity 75%, specificity 73.5%) and operation time (cut-off value 237.5, sensitivity 62.5%, specificity 78.6%).

Conclusions: The FI, preoperative MMSE score, and operation time were independent risk factors for POD in elderly patients after cardiac surgery, with high predictive value observed with the FI and operation time. Cerebral oxygen saturation was associated with POD but was not an independent risk factor.

Clinical Trial Registration: Chinese Clinical Trail Registry, No: chictr2200056038.

KEYWORDS

frailty, cardiopulmonary bypass, tissue oxygen saturation, cardiac surgery, postoperative delirium, near-infrared spectroscopy

Introduction

Frailty is an age-related state of diminished physiological reserve and function that results in increased vulnerability to endogenous and exogenous stressors (1-3). With the increasing prevalence of cardiovascular diseases among elderly patients, the incidence of frailty has been

increasing among cardiac surgical patients of these age groups (4–6). Limitations in withstanding surgical stressors (7) are associated with an increased risk of adverse health outcomes such as surgery-related complications, falls, disability, hospitalization, and mortality (8, 9).

Postoperative delirium (POD) represents an acute neurocognitive complication characterized by fluctuating levels of consciousness (10, 11). It mainly occurs within 2-3 days after surgery (12), and has been considered the most common surgical complication among elderly patients (13). Besides the negative impacts of POD on postoperative recovery, it often results in prolonged hospital stay, increased medical costs, as well as increased risk of patient morbidity and mortality (14). The incidence of POD varies across different types of surgeries. In China, the overall incidence of POD in hospitalized patients older than 65 years of age is 17.1% (15), with cardiac surgery having a 46% incidence of POD due to the intraoperative effects of extracorporeal circulation (16). The etiology of POD is multifactorial (17), and may involve both intrinsic and extrinsic factors such as age, cognitive dysfunction, comorbidities, visual and hearing status, and alcohol use, among others (18, 19).

The aim of the study is to explore the risk factors for POD in frail elderly patients undergoing on-pump cardiac surgery, to further improve the clinical prevention and treatment of POD among such patients.

Methods

Study design

This study was approved by the Institutional Committee for Medical Ethics (2022ky002), and has been registered on the Chinese Clinical Trial Registry (https://www.chictr.org.cn/ ChiCTR2200056038).

Patients undergoing elective on-pump cardiac surgery at Northern Jiangsu People's Hospital (Yangzhou City, Jiangsu province, China) between November 2021 and May 2022 were prospectively enrolled. Inclusion criteria included age \geq 65 years. Exclusion criteria included (1) hepatic or renal insufficiency; (2) not capable of self-care; (3) visual and hearing impairment; (4) history of severe neuropsychiatric illness; (5) recent sedatives or antidepressant use; (6) cerebrovascular diseases such as intracranial aneurysm, head and neck artery stenosis or occlusion, and vascular cognitive impairment, (7) hemorrhagic stroke or traumatic brain injury with sequelae, (8) inability to cooperate with study protocol, (9) preoperative Mini-Mental State Examination (MMSE) score <20, and (10) emergency surgeries.

Perioperative management

Baseline frailty status was assessed using the FI scale. Patients were assessed preoperatively according to the FI, and frailty was defined as FI ≥ 0.25 ; pre-frailty was defined as FI 0.09–0.25. Cerebral oxygen saturation was monitored using the FORE-SIGHT oximeter (CASMED, Branford, CT, USA). Renal and

brachioradialis muscle oxygen saturations were monitored using the INVOS5100C device (Medtronic, Minneapolis, MN).

Study protocol

A single blinded anesthetist was involved in the study, and anesthetic management was not influenced by the oxygen saturation monitoring values. Induction was performed with a single injection of midazolam (0.1-0.5 mg/kg), etomidate (0.1-0.4 mg/kg), sufentanil (0.5 ug/kg), and cisatracurium (0.2 mg/ kg). The pressure-controlled ventilation volume-guaranteed (PCV-VG) mode was used with the following parameters: fraction of inspired oxygen (FiO₂), 0.6-0.8; tidal volume, 6-8 ml/kg (employing ideal body weight); PEEP, 5 cmH₂O; and partial carbon dioxide pressure (PaCO₂), 40 mmHg, as measured using an arterial blood gas analyzer (Gem 3500, Instrumentation Laboratory, Bedford, MA, USA). Maintenance was achieved with dexmedetomidine (0.2-0.5 ug/kg/h), cisatracurium (0.05-0.1 mg/ kg/h), and sevoflurane (1%-2.5%). Sufentanil was administered as necessary throughout the procedure. Noradrenaline, dopamine, dobutamine, and nitroglycerin were used to maintain hemodynamic balance. MAP was maintained within 20% of baseline.

Extracorporeal circulation was performed using a heart-lung machine (MAQUET, Rastatt, Germany) and a membrane oxygenator (TERUMO Corporation, Tokyo, Japan). Heparin (300 U/kg) was administered to achieve an activated coagulation time (ACT) of \geq 480 s. Antegrade hyperkalemic cardioplegia was instituted, and moderate hypothermia was applied (32–35°C). Perfusion flow rate (2.0–2.4 L/min/m²) was adjusted to maintain a perfusion pressure of 60–80 mmHg. Blood pH and hematocrit were maintained at 7.35–7.45 and 25%–30%, respectively. ACT was monitored dynamically, and heparin was added as necessary. Upon completion of the procedure, slow infusion of protamine was administered via the ascending aorta for neutralization.

The FI scale we used assessed 50 items, including mental status, self-care ability, motor coordination, adverse living habits, head and neck diseases, cardiovascular diseases, pulmonary diseases, abdominal diseases, cerebrovascular diseases, hypertension, hyperlipidemia, diabetes, skin diseases, musculoskeletal diseases, sleep quality, physiological and mental illness, cognitive disorders, standing and walking posture, and history of falls. The patient FI was defined as the ratio of the number of items showing defects to the total number of assessed items. The total score was 1. Frailty, pre-frailty, and non-frailty were defined as FI \geq 0.25, FI 0.09–0.25, and FI \leq 0.08, respectively.

Baseline demographic and clinical data included sex, age, body mass index (BMI), noninvasive and invasive blood pressure, the American Society of Anesthesiologist (ASA) score, New York Heart Association (NYHA) classification, MMSE score, presence of comorbidities such as hypertension, diabetes, hyperlipidemia, cerebrovascular disease, intraoperative vasoactive drug doses, hemoglobin, white cell count, albumin, N-terminal pro-B-type natriuretic peptide, S100 β calcium binding protein, left ventricular ejection fraction, left atrium diameter, left ventricle diameter, and surgery type. Intraoperative data included doses of the vasoactive drugs, operation time, mechanical ventilation time, CPB time, aortic cross clamp time, and tissue oxygen saturation. Cerebral (SctO₂), renal (SrtO₂), and brachioradialis muscle oxygen saturation (SmtO₂) were recorded at the following time points: 1 day presurgery (T0), 5 min post-admission (T1), pre-tracheal intubation (T2), 5 min post-tracheal intubation (T3), pre-CPB (T4), at aortic clamp (T5), at aortic clamp opening (T6), the end of CPB (T7), post-surgery (T8), followed by post-surgery day 1 (T9), 3 (T10), 5 (T11), and 7 (T12). The baseline (SctO₂ baseline, SrtO₂ baseline), lowest (SctO₂ lowest, SrtO₂ lowest, SmtO₂ lowest), and greatest (SctO₂ decrease, SrtO₂ decrease, SmtO₂ decrease) oxygen saturation values were recorded.

Postoperative data included complications, as well as cardiac intensive care unit (ICU) and hospital length of stay. The postoperative complications included postoperative pulmonary complications (pneumonia, atelectasis, pulmonary embolism, pulmonary insufficiency), postoperative nausea and vomiting, and sternal wound infections (both deep and superficial infections).

Statistical analysis

All statistical analyses were performed using SPSS version 25. Normality of distribution was assessed using the Kolmogorov-Smirnov test. Normally distributed data are expressed as mean \pm standard deviation (SD), with intra- and inter-group comparisons made using Student *t*-test, respectively. Non-normally distributed data were compared using Mann-Whitney *U*-test. Numerical data were compared using the chi-square test. Risk factors for POD were analyzed using logistic regression, and

their predictive values were assessed using the receiver operating characteristic (ROC) curve analysis.

Sample size estimation

The sample size was calculated with reference to the preliminary study and based on the sample size calculation formula. Since the probability of postoperative delirium was p = 0.6 for group A and p = 0.3 for group B, then for equal N in each group, $\alpha = 0.05$, and $(1-\beta) = 0.90$, the required sample size was N = 112.

Results

Patient characteristics

A total of 145 patients were scheduled for on-pump cardiac surgery during the study period (Figure 1). Among them, 15 were excluded due to FI <0.1 (n = 10), and death within 7 days of surgery (n = 5). As such, 130 patients were eventually included for data analysis.

Univariate logistic regression analysis results of potential clinical and demographic risk factors

A total of 32 patients (24.6%) demonstrated POD. The clinical data of the POD and Non-POD groups are summarized in Table 1.



TABLE 1 Univariate logistic regression analysis results of potential clinical and demographic risk factors.

		Non-POD (<i>n</i> = 98)	POD (<i>n</i> = 32)	<i>P</i> -value	
Age [year, (Q1, Q3)]		67 (64–72.3)	68 (60-74)	0.965	
Sex, n (%) M		60 (61.2%)	16 (50%)	0.237	
	F	38 (38.8%)	16 (50%)	-	
ASA, n (%)	IV	95 (96.9%)	29 (90.6%)	0.143	
	V	3 (3.1%)	3 (9.4%)		
NYHA, n (%)	Ш	32 (32.7%)	6 (18.8%)	0.125	
	IV	66 (67.3%)	26 (81.3%)		
BMI $[kg/m^2, (x \pm s)]$		22.7 ± 3.5	22.6 ± 3.6	0.925	
Frailty, n (%)	Pre-frail	72 (73.4%)	8 (25%)	<0.001	
	Frail	26 (26.5%)	24 (75%)		
Preoperative MMSE		23 (21.8–25)	21.5 (20–22)	< 0.001	
Postoperative MMSE		23 (21–25)	22 (20–23.8)	0.075	
Preoperative morbidi	itv. n (%)				
Typertension	, , (, .,	57 (58.1%)	24 (24.7%)	0.081	
Hyperlipidemia		8 (8.2%)	9 (6.9%)	0.004	
Diabetes mellitus		11 (11.3%)	11 (8.5%)	0.004	
Cerebrovascular disease		32 (33.0%)	19 (14.6%)	0.008	
	of the vacestive day			0.000	
-	of the vasoactive dru		0.74 (0.2, 1.20)	0.222	
Norepinephrine		0.8 (0.41-1.28) 7.1 ± 3.1	0.74 (0.3–1.29)	0.322	
Dopamine		/.1 ± 3.1	7.7 ± 3.2	0.289	
Biochemical indices				1	
Hemoglobin (g/L)		12.7 (11.6–14.1)	11.5 (8.9–12.6)	<0.001	
White blood cell (×10 ⁹ /L)		5.7 (4.5-7.4)	6.4 (4.7–8.7)	0.289	
Albumin (g/L)		38.9 (35.7-42.7)	38.9 (35.7–42.7) 37.0 (32.4–39)		
Serum creatinine (umol/L)		81.2 (70.5-97.9)	91 (70.5–124.3)	0.088	
NT-proBNP (pg/ml)		711 (219.8–2,243)	1,474 (416.8–3,359)	0.055	
cTnI (ng/ml)		1.4 (0.2–2.6)	0.8 (0.2–2.6)	0.97	
CK-MB (ng/ml)		14.2 (2.6–20.7) 13.8 (2.4–22.2)		0.756	
S100β protein (μg/L)					
T1		0.16 (0.09-0.24)	0.19 (0.14-0.25)	0.263	
Т9		0.22 (0.15-0.32)	0.37 (0.21-0.63)	0.072	
Т10		0.22 (0.12-0.31)	0.26 (0.17-0.40)	0.072	
T11		0.23 (0.14-0.31)	0.23 (0.14-0.32)	0.918	
Т12		0.24 (0.14–0.35)	0.22 (0.14-0.30)	0.359	
The operation type, <i>i</i>	n (%)				
Valve		58 (59.2%)	13 (40.6%)	0.151	
CABG		13 (13.3%)	10 (31.3%)		
Aortic		7 (7.1%)	3 (9.4%)		
Combination		9 (9.2%)	4 (12.5%)		
Others		11 (11.2%)	2 (6.3%)	-	
Echocardiography ind	dices				
LVEF (%)		57 (48-60)	52.5 (42-60.8)	0.272	
LVEF (%) LAd (mm)		43 (39-49.3)	43 (39.3-48)	0.272	
LVd (mm)		53 (48-60.3)		0.489	
		33 (40-00.3)	55 (47.3-61.8)	0.489	
Time indices					
Operation time (min)		192.5 (175–230)	262.5 (197.5–327.5)	<0.001	
CPB time (min)		79 (70–105)	98.5 (68.8–124)	0.021	
Aortic cross clamp time (n		51 (40-75)	59 (42.3-89.8)	0.211	
Mechanical ventilation tim		10 (7–15)	9.5 (8-14.8)	0.963	
The length of stay in CICU		4 (3-5.3)	4 (3-6.8)	0.679	
The length of stay in hospital (days)		22.5 (19-27.3)	23 (18-30)	0.957	

ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; BMI, body mass index; MMSE, mini-mental state examination; cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; CM-MB, creatine kinase-MB; CABG, coronary artery bypass grafting; CPB, cardio-pulmonary bypass.

TABLE	2	Results	of	univariate	logistic	regression	analysis	of	potential
tissue oxygen saturation risk factors.									

	Non-POD (<i>n</i> = 98)	POD (<i>n</i> = 32)	<i>P</i> -value
SctO ₂			
TO	65 (62–68)	64 (60-67.8)	0.05
T1	64.5 (62-70)	64 (58-68)	0.06
T2	68.4 ± 4.9	65.4 ± 5.2	0.004
T3	67 (64–73)	66.5 (62.3-70)	0.269
T4	65.3 ± 6.1	63.4 ± 6.2	0.137
T5	66.2 ± 5.9	65.3 ± 6.8	0.435
T6	64.5 (62–68)	64 (62–67)	0.296
T7	64 (61.8-68)	64 (61.3-66.8)	0.778
T8	66.5 (64–69.3)	64 (62–69.8)	0.169
Т9	66 (64–70)	64 (61.3-67.8)	0.018
T10	66.5 (64-71.3)	65 (62–69.5)	0.147
T11 T11	66 (63-70)	64.5 (62–68)	0.209
T12	65.5 (63.8–70)	66 (62.3–69.8)	0.981
SctO _{2baseline}	65 (62.5-69)	63.5 (59-68)	0.05
SctO _{2baseline}	59 (57-62)	55 (49.3-59)	<0.001
SctO _{2lowest}	9.4 (6.2–13.9)	9.5 (5.3-22.4)	0.392
	5.4 (0.2-13.7)	9.5 (5.5-22.4)	0.372
SmtO ₂		1	
Т0	66.4 ± 10.4	67.5 ± 10.5	0.584
T1	64 ± 10.9	63.5 ± 10.2	0.798
T2	66.4 ± 10.4	67.5 ± 10.5	0.584
T3	63.7 ± 8.9	64 ± 8	0.849
T4	62 (53-68.3)	62 (55-66.5)	0.858
T5	62 (51.8-68)	61 (53.5-64)	0.49
T6	64.3 ± 10.8	61.8 ± 9.8	0.238
T7	64 (59-72.3)	61.5 (52.3-69)	0.206
T8	67 (62-72)	65.5 (60-69.8)	0.073
Т9	64.6 ± 10.1	63.3 ± 8.5	0.49
T10	66.8 ± 10.1	63.2 ± 6.8	0.059
T11	66.1 ± 9	64.3 ± 8.3	0.306
T12	66.8 ± 8.8	65.3 ± 6.8	0.36
SmtO _{2baseline}	65.2 ± 9.9	65.5 ± 9.7	0.881
SmtO _{2lowest}	51.5 (48-59.3)	52 (49-57.8)	0.657
SmtO _{2decrease}	14.5 (6.6-26.9)	17.5 (6.3–28.4)	0.865
SrtO ₂			
Т0	69 (66.8–75)	68 (64.3-72)	0.268
T1	68.7 ± 6.5	67.9 ± 6.4	0.571
T2	69 (66.8–75)	68 (64.3-72)	0.268
T3	68 (65-72)	65.5 (64.3-70)	0.192
T4	66.5 (63.8-73)	67 (64-69.8)	0.647
T5	67 (63-73.5)	65 (62.5-70.8)	0.526
T6	67 (62–72)	65.5 (62-68)	0.245
T7	67 (61.8–72)	64.5 (62-69)	0.316
T8	69.1 ± 6.6	68.1 ± 4.2	0.426
Т9	66.1 ± 5.4	66.7 ± 5.8	0.572
T10	67 (63-72)	67 (62–72)	0.598
T11	67 ± 6.1	67.7 ± 6.8	0.598
T12	66.9 ± 6.2	66.8 ± 6.1	0.972
SmtO _{2baseline}	69.2 ± 5.6	68.2 ± 5.3	0.356
SmtO _{2lowest}	60.5 (56-62)	59 (56.3-62)	0.374
SmtO _{2decrease}	12.8 (6.8–18.0)	11.3 (8.3–16.9)	0.976
	. ,		

 ${\rm SctO}_2,$ cerebral oxygen saturation; ${\rm SrtO}_2,$ renal oxygen saturation; ${\rm SmtO}_2,$ brachioradialis oxygen saturation.

TABLE 3 Results of multivariate logistic regression analysis.

	OR	95% CI		P-value
Frailty	0.27	0.063	0.909	0.036
Preoperative MMSE	0.71	0.528	0.954	0.023
Operation time	1.012	1.002	1.022	0.015

MMSE, mini-mental state examination.





Based on univariate analysis, the FI, preoperative MMSE score, hyperlipidemia, diabetes mellitus, cerebrovascular disease, hemoglobin and albumin levels, operation time and CPB time were found as significant risk factors for POD (Table 1).

Tissue oxygen saturation

 $SctO_2$ (T₂), and $SctO_{2lowest}$ were found as significant risk factors for POD. The two groups showed no statistically significant difference in $SrtO_2$ and $SmtO_2$ (Table 2).

Multivariate logistic regression analysis

Only the FI (OR 0.27, 95% CI 0.063–0.909), preoperative MMSE score (OR 0.71, 95% CI 0.528–0.954), and operation time (OR 1.012, 95% CI 1.002–1.022) remained significant in the multivariate analysis (P < 0.05) (Table 3).

The FI (AUC 0.742, 95% CI 0.642–0.843, P < 0.001), preoperative MMSE score (AUC 0.281, 95% CI 0.184–0.378, P < 0.001), and operation time (AUC 0.751, 95% CI 0.652–0.849, P < 0.001) were found as significant predictive factors for POD (Figure 2). Both sensitivity and specificity were high for the FI (cut-off value, 0.27; sensitivity, 75%; specificity, 73.5%) and operation time (cut-off value, 237.5; sensitivity, 62.5%; specificity, 78.6%). However, while the sensitivity for the preoperative MMSE score was high, the specificity was found to be 0% (cutoff value, 19; sensitivity, 100%, specificity, 0%).

Discussion

Among the elderly patients undergoing elective on-pump cardiac surgery, 50 (38.5%) were considered frail at baseline, and demonstrated a POD incidence of 46%. This is in contrast with the 80 (61.5%) pre-frailty patients, who demonstrated a POD incidence of 11.3%, which was significantly lower. The pathogenesis of frailty is multifactorial, and can be the result of chronic diseases, unhealthy lifestyles, and activity limitation. The reduced physiological reserve, coupled with the impaired resistance to surgical stress, thereby render a poor prognosis inevitable among frail patients (20, 21). In line with this, patients of the frailty group demonstrated greater comorbidities at baseline. Such patients further associated with lower cardiac function grades, which corroborated with the need for significantly higher doses of intraoperative dopamine compared to their counterparts. In addition, the rate of postoperative pulmonary complications was significantly higher among frail patients. Frail patients also reported longer length of hospital stay. Although statistically insignificant, this implied a longer recovery duration among such patients.

Frailty was demonstrated to significantly associate with POD in our study. Frailty was assessed in terms of FI, which employs a cumulative deficits approach, and has been considered an effective predictor of adverse outcome (22). As reported in the meta-analysis by Kojima et al., every 0.1 increase in FI was associated with a 28% increase in mortality risk (23). Importantly, our study found frailty as both an independent risk factor and a predictive factor for POD following cardiac surgery. In general, our findings fit with those of prior research. Although our study did not explore the association of frailty with postoperative mortality, both the operation time and postoperative pulmonary complication rate were higher in patients of the frailty group than those of the pre-frailty group, which may also be predictive of poor outcomes in patients with frailty.

The exposure of blood to foreign material during extracorporeal circulation may precipitate widespread inflammatory responses which can lead to postoperative neurocognitive decompensation (24). Hemodynamic fluctuations involved during CPB may further disrupt the perfusion of brain tissues and result in cerebral ischemia, one of the risk factors of POD (25). Conventional arterial pressure monitoring techniques such as MAP have been considered inadequate for the accurate reflection of cerebral perfusion (26, 27). Near-infrared spectroscopy (NIRS) is an emerging noninvasive brain imaging technology that is portable, mobile, and low-cost (28). It utilizes near-infrared light from 650 to 900 nm to determine cerebral oxygenation, blood flow, and metabolic status of localized regions of the brain. NIRS enables the continuous monitoring of rSO2, which allows for timely detection of cerebral hypoxia, and thereby plays an essential role in the protection against POD (29). In the observational study by Eertmans et al. (30) involving the continuous monitoring of rSO₂ until 72 h after cardiac surgery, higher EuroSCORE II, lower preoperative MMSE score, and greater decrease in absolute postoperative rSO₂ independently associated with POD. Our findings were partly in line with this, with frailty and the preoperative MMSE score identified as significant risk factors for POD, in addition to operation time. In contrast, SctO₂ (T2) and SctO_{2lowest} did not demonstrate significant association to POD on multivariate analysis. This may be due to the small sample size of our study, which rendered insufficient statistical power, and the relatively short duration of monitoring. Renal oxygen saturation (SrtO₂) has been often used to monitor the renal tissue blood perfusion to determine the presence of renal ischemia and hypoxia and to prevent the occurrence of acute renal injury (31). Simultaneously, other studies have described the monitoring the oxygen saturation of muscle tissue to assess the level of lactic acid in patients and thereby predict the body perfusion of patients (32). These results suggest that the oxygen saturation of renal and muscle tissue can reflect the blood perfusion level and oxygencarrying capacity of the body to a certain extent. Our study show that the two groups showed no statistically significant difference in SrtO₂ and SmtO₂. SrtO₂ and SmtO₂ were not significant risk factors for POD.

Several studies have similarly identified operation time as a risk factor for cognitive dysfunction following surgery (33, 34). Prolonged duration of surgery not only increases the dosage of anesthetic drugs, but also increases the risk of cerebral ischemia and hypoxia (35). Our findings of an operation time of >237.5 min as an independent risk factor highlighted the importance of establishing a reasonable surgical plan to minimize the duration of surgery for the prevention of POD among frail elderly patients undergoing cardiac surgery.

There were several other limitations to this study. First, our results were limited by the single-center observational design. Second, as only cardiac surgeries involving extracorporeal circulation were considered, procedures such as off-pump coronary artery bypass grafting and aortic dissection were overlooked, thereby limiting the applicability of our results. Multi-center large-sample studies evaluating the association of frailty with POD following a wider range of cardiac surgeries are therefore warranted.

In summary, the FI, preoperative MMSE score, and operation time were independent risk factors for POD in elderly patients after cardiac surgery, with the FI and operation time showing a high predictive value, Cerebral oxygen saturation was associated with POD but was not an independent risk factor. Renal oxygen saturation and muscle oxygen saturation were not significant risk factors for POD.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/Supplementary Material.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Northern Jiangsu People's Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

YD: Software, Writing – original draft. JG: Conceptualization, Funding acquisition, Investigation, Writing – review & editing. YG: Data curation, Writing – review & editing. TH: Project administration, Writing – review & editing. YZ: Funding acquisition, Writing – review & editing.

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References

1. Cloney MB, Ordon M, Tecle NE, Sprau A, Kemeny H, Dahdaleh NS. Frailty predicts readmission, reoperation, and infection after posterior spinal fusion: an institutional series of 3,965 patients. *Clin Neurol Neurosurg.* (2022) 222:107426. doi: 10.1016/j.clineuro.2022.107426

2. Beier F, Loffler M, Nees F, Hausner L, Frolich L, Flor H. Sensory and motor correlates of frailty: dissociation between frailty phenotype and frailty index. *BMC Geriatr.* (2022) 22(1):755. doi: 10.1186/s12877-022-03416-6

3. Fowler AJ, Stephens TJ, Partridge J, Dhesi J. Surgery in older patients: learning from shared decision-making in intensive care. *Br J Anaesth*. (2022) 129(5):652–5. doi: 10.1016/j.bja.2022.08.002

4. Sun LY, Jabagi H, Fang J, Lee DS. Comparison of multidimensional frailty instruments for estimation of long-term patient-centered outcomes after cardiac surgery. *JAMA Netw Open*. (2022) 5(9):e2230959. doi: 10.1001/jamanetworkopen. 2022.30959

5. Miguelena-Hycka J, Lopez-Menendez J, Prada PC, Garcia MM, Vigil-Escalera C, Harmand MG, et al. Changes in frailty status after cardiac surgery. A prospective cohort study. *Arch Gerontol Geriatr.* (2022) 98:104568. doi: 10.1016/j.archger.2021. 104568

6. Bielecka-Dabrowa A, Ebner N, Dos Santos MR, Ishida J, Hasenfuss G, von Haehling S. Cachexia, muscle wasting, and frailty in cardiovascular disease. *Eur J Heart Fail.* (2020) 22(12):2314–26. doi: 10.1002/ejhf.2011

7. Miura Y, Nishio K, Kitamura Y, Goto T, Yano M, Matsui S. Surgical risk assessment for super-elderly patients. *Geriatr Gerontol Int.* (2022) 22(4):271–7. doi: 10.1111/ggi.14340

8. Emmert DA, Arcario MJ, Maranhao B, Reidy AB. Frailty and cardiac surgery: to operate or not? *Curr Opin Anaesthesiol.* (2022) 35(1):53–9. doi: 10.1097/ACO. 000000000001075

9. Lal S, Gray A, Kim E, Bunton RW, Davis P, Galvin IF, et al. Frailty in elderly patients undergoing cardiac surgery increases hospital stay and 12-month readmission rate. *Heart Lung Circ.* (2020) 29(8):1187–94. doi: 10.1016/j.hlc.2019.10. 007

10. Mossello E, Baroncini C, Pecorella L, Giulietti C, Chiti M, Caldi F, et al. Predictors and prognosis of delirium among older subjects in cardiac intensive care unit: focus on potentially preventable forms. *Eur Heart J Acute Cardiovasc Care.* (2020) 9(7):771–8. doi: 10.1177/2048872619882359

11. Tsai CY, Liu KH, Lai CC, Hsu JT, Hsueh SW, Hung CY, et al. Association of preoperative frailty and postoperative delirium in older cancer patients undergoing elective abdominal surgery: a prospective observational study in Taiwan. *Biomed J.* (2022) 46(4):100557. doi: 10.1016/j.bj.2022.08.003

12. Fong TG, Inouye SK. The inter-relationship between delirium and dementia: the importance of delirium prevention. *Nat Rev Neurol.* (2022) 18(10):579–96. doi: 10. 1038/s41582-022-00698-7

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Conflict of interest

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13. Liu H, Zhao Q, Liu X, Hu X, Wang L, Zhou F. Incidence and interaction factors of delirium as an independent risk of mortality in elderly patients in the intensive units: a retrospective analysis from MIMIC-IV database. *Aging Clin Exp Res.* (2022) 34(11):2865–72. doi: 10.1007/s40520-022-02215-8

14. Sato K, Kubota K, Oda H, Taniguchi T. The impact of delirium on outcomes in acute, non-intubated cardiac patients. *Eur Heart J Acute Cardiovasc Care*. (2017) 6 (6):553–9. doi: 10.1177/2048872615624239

15. Zhang M, Zhang X, Gao L, Yue J, Jiang X. Incidence, predictors and health outcomes of delirium in very old hospitalized patients: a prospective cohort study. BMC Geriatr. (2022) 22(1):262. doi: 10.1186/s12877-022-02932-9

16. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. (2014) 383(9920):911-22, doi: 10.1016/S0140-6736(13)60688-1

17. Wilcox ME, Girard TD, Hough CL. Delirium and long term cognition in critically ill patients. *Br Med J.* (2021) 373:n1007. doi: 10.1136/bmj.n1007

18. Gravante F, Giannarelli D, Pucci A, Gagliardi AM, Mitello L, Montagna A, et al. Prevalence and risk factors of delirium in the intensive care unit: an observational study. *Nurs Crit Care.* (2021) 26(3):156–65. doi: 10.1111/nicc.12526

19. Kazmierski J, Miler P, Pawlak A, Jerczynska H, Nowakowska K, Walkiewicz G, et al. Increased postoperative myeloperoxidase concentration associated with low baseline antioxidant capacity as the risk factor of delirium after cardiac surgery. *Ann Med.* (2022) 54(1):610–6. doi: 10.1080/07853890.2022.2039405

20. Kjelsnes AA, Feiring E. Models of integrated care for older people with frailty: a horizon scanning review. *BMJ Open.* (2022) 12(4):e060142. doi: 10.1136/bmjopen-2021-060142

21. Kalyanasundaram A, Li N, Gardner ML, Artiga EJ, Hansen BJ, Webb A, et al. Fibroblast-specific proteotranscriptomes reveal distinct fibrotic signatures of human sinoatrial node in nonfailing and failing hearts. *Circulation*. (2021) 144(2):126–43. doi: 10.1161/CIRCULATIONAHA.120.051583

22. Barker FJ, Davies JI, Gomez-Olive FX, Kahn K, Matthews FE, Payne CF, et al. Developing and evaluating a frailty index for older South Africans-findings from the HAALSI study. *Age Ageing.* (2021) 50(6):2167–73. doi: 10.1093/ageing/afab111

23. Khalafallah AM, Huq S, Jimenez AE, Brem H, Mukherjee D. The 5-factor modified frailty index: an effective predictor of mortality in brain tumor patients. *J Neurosurg.* (2020) 135(1):78-86. doi: 10.3171/2020.5.JNS20766

24. Hatami S, Hefler J, Freed DH. Inflammation and oxidative stress in the context of extracorporeal cardiac and pulmonary support. *Front Immunol.* (2022) 13:831930. doi: 10.3389/fimmu.2022.831930

25. Qin XW, Chen XL, Yao L. The value of intraoperative monitoring of cerebral oxygen saturation on postoperative cognitive function in elderly patients undergoing cardiac surgery. *Zhonghua Yi Xue Za Zhi.* (2021) 101(5):345–9. doi: 10. 3760/cma.j.cn112137-20200527-01681

26. Christie IN, Windsor R, Mutsaerts HJ, Tillin T, Sudre CH, Hughes AD, et al. Cerebral perfusion in untreated, controlled, and uncontrolled hypertension. J Cereb Blood Flow Metab. (2022) 42(12):2188–90. doi: 10.1177/0271678X221124644

27. Liu X, Nakano M, Yamaguchi A, Bush B, Akiyoshi K, Lee JK, et al. The association of bispectral index values and metrics of cerebral perfusion during cardiopulmonary bypass. J Clin Anesth. (2021) 74:110395. doi: 10.1016/j.jclinane.2021.110395

28. Mihara M, Miyai I. Review of functional near-infrared spectroscopy in neurorehabilitation. *Neurophotonics*. (2016) 3(3):031414. doi: 10.1117/1.NPh.3.3. 031414

29. Tribuddharat S, Ngamsaengsirisup K, Mahothorn P, Sathitkarnmanee T. Correlation and agreement of regional cerebral oxygen saturation measured from sensor sites at frontal and temporal areas in adult patients undergoing cardiovascular anesthesia. *PeerJ.* (2022) 10:e14058. doi: 10.7717/peerJ.14058

30. Eertmans W, De Deyne C, Genbrugge C, Marcus B, Bouneb S, Beran M, et al. Association between postoperative delirium and postoperative cerebral oxygen desaturation in older patients after cardiac surgery. *Br J Anaesth.* (2020) 124 (2):146–53. doi: 10.1016/j.bja.2019.09.042

31. Bonsante F, Ramful D, Binquet C, Samperiz S, Daniel S, Gouyon JB, et al. Low renal oxygen saturation at near-infrared spectroscopy on the first day of life is associated with developing acute kidney injury in very preterm infants. *Neonatology.* (2019) 115(3):198–204. doi: 10.1159/000494462

32. Lee YS, Kim WY, Yoo JW, Jung HD, Min TJ. Correlation between regional tissue perfusion saturation and lactate level during cardiopulmonary bypass. *Korean J Anesthesiol.* (2018) 71(5):361–7. doi: 10.4097/kja.d.17.00002

33. Kang T, Park SY, Lee JH, Lee SH, Park JH, Kim SK, et al. Incidence & risk factors of postoperative delirium after spinal surgery in older patients. *Sci Rep.* (2020) 10 (1):9232. doi: 10.1038/s41598-020-66276-3

34. Zhang G, Wang Z, Wang D, Jia Q, Zeng Y. A systematic review and metaanalysis of the correlation between operation time and postoperative delirium in total hip arthroplasty. *Ann Palliat Med.* (2021) 10(10):10459–66. doi: 10.21037/ apm-21-2190

35. Baek W, Kim YM, Lee H. Risk factors of postoperative delirium in older adult spine surgery patients: a meta-analysis. *AORN J.* (2020) 112(6):650–61. doi: 10.1002/aorn.13252