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Evaluation of postoperative delirium in cardiac surgery patients with the SDACS screening tool: a multicenter-multiphase study

Hosein Mahmoudi[1], Athanasios Chalkias[2,3], Ali Moradi[1], Seyed Tayeb Moradian[1], Seyed Mohammad Reza Amouzegar[4] and Amir Vahedian-Azimi[1*]

Abstract

Objective Postoperative delirium is a prevalent complication in cardiac surgery patients, highlighting the importance of early risk factor identification for optimal management. This study aimed to pinpoint risk factors and devise a novel screening tool, the Screening Tool for Delirium After Cardiac Surgery (SDACS), to predict postoperative delirium in cardiac surgery patients after the first day.

Materials and methods This study employed a multiphase design consisting of three phases. In the first phase, through a scoping review of 38 finally selected published papers, 136 potential risk factors for identifying delirium after cardiac surgery were identified. These risk factors were then incorporated into three Delphi rounds of expert panels to develop a screening tool for postoperative delirium. Finally, 76 potential risk factors were examined on 920 cardiac surgery patients at three academic institutions between 2020 and 2023 (third phase of the study). All predictors were included into a screening instrument (SDACS), and the regression coefficient of each predictor was transformed into a risk score.

Results Delirium was diagnosed in 53% ($n=488$) of 920 patients. Four independent predictors of delirium were identified: chronic opioid use (*OR*: 4.605, 95% *CI*: 2.163–9.804), hearing impairment (*OR*: 6.926, 95% *CI*: 3.630–12.215), benzodiazepine history (*OR*: 8.506, 95% *CI*: 5.651–11.805), and poor sleep quality on the first night after cardiac surgery (*OR*: 9.081, 95% *CI*: 6.225–12.248). The cross-validated area under receiver operating characteristics curve (AUC) for the screening instrument was 0.897 (95% *CI*: 0.876–0.916; $P<0.001$).

Conclusion Chronic opioid use, hearing impairment, benzodiazepine history, and poor sleep quality post-surgery are linked to postoperative delirium in cardiac surgery patients. The SDACS screening tool effectively forecasts this syndrome early, offering bedside nurses a valuable tool for prompt intervention and improved patient outcomes. The SDACS screening tool aids in early delirium risk assessment, enabling timely interventions and better patient outcomes. By predicting postoperative delirium accurately, nurses can address risk factors proactively, potentially reducing its incidence and severity, leading to improved postoperative outcomes for patients.

Keywords Cardiac surgery, Delirium, Early prediction, Screening tool, Intensive care, Critical care

*Correspondence:
Amir Vahedian-Azimi
amirvahedian63@gmail.com
Full list of author information is available at the end of the article

Introduction

Delirium, a sudden, fluctuating, and usually reversible disturbance of mental function, is a common complication after cardiac surgery and often goes undiagnosed. Its reported prevalence ranges from 4.1 to 54.9% in this population, making it a global public health burden (Chen et al. 2021; Koster et al. 2013; Rahimi-Bashar et al. 2021). Delirium is strongly associated with an increased incidence of other postoperative complications, including cognitive decline, prolonged mechanical ventilation (MV), prolonged hospital and intensive care unit (ICU) stay, and increased healthcare costs (Bashar et al. 2018; Vahedian Azimi et al. 2015). In severe cases, delirium may also contribute to higher in-hospital mortality and long-term mortality after discharge (Gosselt et al. 2015; Koster et al. 2011; O'Neal et al., 2017).

The invasive nature of cardiac surgery, along with the physiological stressors experienced by patients, increases the risk of delirium during the postoperative period (Kumar 2020; Sarkar and Prabhu 2017). However, the pathophysiology of delirium is complex and not fully understood, and several incriminating causes are reported in literature (Cerejeira et al. 2010). Cardiopulmonary bypass (CPB), commonly used in cardiac surgery, induces systemic inflammation that leads to endothelial dysfunction and disruption of the blood–brain barrier (Rudolph et al. 2008; van Harten et al. 2012). This, in turn, triggers neuroinflammation and activation of microglial cells. It is worth noting that several randomized controlled studies have shown that shortening the duration of (a diagnosed) delirium through clinical intervention does not effectively reduce short-term mortality (Al-Qadheeb et al. 2014).

Although the likelihood of developing delirium increases with the presence of multiple risk factors, limited research has focused on predicting its development, and the existing prediction screening tools lack sufficient accuracy (Andrási et al., 2022; den Boogaard et al. 2024; Satomoto 2023; Xu et al. 2022). By identifying patients at higher risk, targeted interventions can be implemented to address these factors and potentially reduce the frequency and severity of delirium. As the prevention or early detection of delirium remains a crucial area of clinical research, we conducted a multicenter, multiphase study to determine predictive risk factors and develop a screening tool for early prediction of delirium after cardiac surgery.

Material and methods

Study design

This study utilized a three-phase design. In the initial phase, a scoping review was conducted to identify risk factors linked to delirium after cardiac surgery. A comprehensive search was conducted across PubMed/MEDLINE, Scopus, Web of Science, and ProQuest databases, resulting in 5832 relevant articles. Moreover, a bibliographic review was performed, yielding 77 additional relevant articles. Based on strict inclusion and exclusion criteria, as well as a detailed review by two independent researchers, the final selection was narrowed down to 38 relevant studies (Supplementary File 1, Fig. S1).

The second phase of the study involved a Delphi survey consisting of three consecutive face-to-face rounds. A total of 136 potential risk factors, identified from the 38 studies, and their applicability in daily clinical practice, were evaluated in three Delphi consensus validation rounds including experts on perioperative and critical care medicine. The first two rounds identified potential predictors that were reasonably reproducible and relatively easy to assess in a heterogeneous population of cardiac surgery patients. The methods for the first and second phases have recently been published (Moradi et al. 2022). All comments from the first round were available to the participants in the second round. In the third Delphi round, experts aimed to identify risk factors that align with common treatment, diagnosis, and care approaches. All comments from the second round were available to the participants in the third round.

In the third phase of the study, 76 potential risk factors were selected based on consensus from expert panels during the Delphi rounds. These factors were examined in a cross-sectional study involving 920 patients who underwent cardiac surgery, with the aim of developing a novel screening tool for the early prediction of postoperative delirium. The design of the present multiphase study is depicted in the Supplementary File 1 (Fig. S2).

Ethical approval

Ethical approval for this study (IR.BMSU.BAQ.REC.1400.052) was provided by the Ethical Committee of Baqiyatallah University of Medical Sciences, Tehran, Iran, on 21 December 2021. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki (Helsinki, 2013), and written informed consent was obtained from all patients or their relatives. The collected data did not contain any patient identifiers to ensure confidentiality and anonymity. The data were stored securely using encrypted databases, accessible only to authorized personnel involved in the research. Personal data were retained only as long as necessary for the research purposes and were scheduled for destruction once they were no longer required. The manuscript adheres to the guidelines provided by the "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement" to ensure transparency and

thorough reporting of the study's methods and results (Vandenbroucke et al. 2014).

Study population

A convenience sampling approach was utilized to recruit eligible adult patients who underwent elective or emergency cardiac surgery at Baqiyatallah Hospital, Rajaei Heart Hospital, and Tehran Heart Center Hospital between 2020 and 2023. The following inclusion criteria were applied preoperatively: (a) hemodynamically stable patients and (b) awake patients with a normal neurological examination. Exclusion criteria were as follows: (a) patients admitted to the ICU before surgery; (b) patients who experienced severe adverse events, such as cardiac arrest or cardiopulmonary resuscitation, during surgery; (c) patients who developed perioperative neurological complications; and (d) patients who were hospitalized or readmitted to the ICU after surgery.

Sample size

To address the inclusion of multiple risk factors and their varying significance in relation to delirium, we utilized the methodology outlined by Peduzzi to estimate the sample size (Peduzzi et al. 1996). Specifically, we took into consideration the incorporation of dummy variables, the dichotomous outcome variable, and the requirement of having at least 10 events per variable. By creating six dummy variables (representing three strata each for type of surgery and blood transfusion) and incorporating delirium as a variable, we initially determined a sample size of 760 patients. To accommodate potential patient dropout and protocol deviations, we adjusted the sample size by 15%, resulting in a final calculated sample size of 874 subjects.

Pre- and postoperation standard delirium evaluation

The standard institutional protocols were followed for aspects such as preoperative evaluation, premedication, and anesthetic and surgical techniques, without any modifications for the participants. This includes careful selection of anesthetic techniques, vigilant hemodynamic management, and early extubation practices aligned with current guidelines that are as follows:

(1) Premedication: Anxiolytics may be used to reduce anxiety preoperatively. However, care is taken to minimize sedative use to reduce the risk of postoperative delirium.
(2) Anesthesia (inhalational anesthesia vs. total intravenous anesthesia (TIVA): Both techniques are utilized based on patient factors and surgical requirements. TIVA is often preferred for its potential to reduce postoperative delirium, particularly in elderly patients, due to less residual sedation.
(3) Neuromonitoring: Neuromonitoring techniques, such as processed electroencephalogram (EEG), may be employed to assess the depth of anesthesia and minimize the risk of awareness and postoperative cognitive dysfunction.
(4) Dexmedetomidine: This medication is increasingly used for its sedative and analgesic properties. It can help maintain sedation without respiratory depression and has been shown to reduce the incidence of delirium postoperatively.
(5) Institutional guidelines on hemodynamic management during CPB: Guidelines typically emphasize maintaining stable hemodynamics with adequate perfusion pressures. This includes (a) monitoring of cardiac output and systemic vascular resistance and (b) use of inotropes or vasopressors as needed to support hemodynamics during and after cardiopulmonary bypass (CPB).
(6) Time to extubation: Early extubation is encouraged when clinically feasible, typically within 6-h postsurgery, as prolonged ventilation is associated with a higher risk of delirium. Protocols are in place to assess readiness for extubation based on hemodynamic stability, respiratory function, and neurological status. Prior to commencing the study, a specialized ICU nurse and a researcher underwent extensive training to identify postoperative delirium using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (Ely et al. 2001). The CAM-ICU is specifically designed to screen for the presence of delirium (not its severity) in critically ill patients, including those on mechanical ventilation, with a sensitivity of 75.5% and specificity of 95.8% (Ely et al. 2001; Neto et al. 2012). The diagnosis of CAM-ICU primarily relies on four key criteria: (a) sudden onset and fluctuating nature of the condition, (b) impaired attention and concentration, (c) disorganized thinking, and (d) altered consciousness. If a patient exhibits both criteria (a) and (b), the presence of either criterion (c) or (d) can be indicative of delirium (Inouye et al. 2014).

Immediately after cardiac surgery, all patients remained intubated and mechanically ventilated and were transferred to the ICU for monitoring and weaning. After the first postoperative day, all patients were assessed twice daily for postoperative delirium using the CAM-ICU. Patients who had at least one delirium event per day were considered as delirium positive. The inter-rater reliability between the assessors was assessed using the kappa

agreement test, with a substantial agreement defined as a kappa value between 0.61 and 0.80 (McHugh, 2012).

Data collection

Data were collected from medical records, anesthesia charts, and perfusion charts (Supplementary File 2) and stored in a predesigned Excel spreadsheet:

(a) Preoperative factors: (1a) Demographic characteristics: age, gender, marriage status, and family support (assessed based on the level of support and presence of family members/friends at the patient's bedside), defined as family bedside presence ≥ 2 h daily (Khaleghparast et al. 2015), categorizing patients into two groups: those who receive support from their family/friends and those who lack this support, body mass index (BMI), education level, smoking status, and addiction history; (2a) preoperative clinical characteristics: comorbidities, based on Charlson Comorbidity Index (CCI) (Charlson et al. 2022), severity of illness based on the Acute Physiology and Chronic Health Evaluation (APACHE) II (Wagner and Draper, 1984), EuroSCORE (Nashef et al. 1999), the presence of metabolic syndrome (Fahed et al., 2022), peripheral vein/arterial disease, ejection fraction rate, carotid status, nutrition status based on the Subjective Global Assessment (SGA) (da Silva Fink et al., 2015), angiography history, Parkinson's disease history, sleep disorder history, psychiatric disorder history (if patients reported prior episodes of depression, stress, or anxiety, a psychiatric diagnosis was stated in the medical charts), speech problem history, visual impairment history, hearing impairment history, admission history, and diagnosis of coronary artery disease (CAD) or valve impairments; (3a) preoperative laboratory data including hematocrit (Hct) and creatinine (Cr) levels; and (4a) preoperative medication data including history of atorvastatin, warfarin, and benzodiazepine treatment.

(b) Intraoperative factors: (1b) Intraoperative clinical characteristics: type of surgery (elective or emergency), grafts used, duration of surgery, CPB surgery, duration of CPB, duration of aortic clamp, main arterial pressure (MAP) during CPB, partial pressure of oxygen (PaO_2) during CPB, use of hypothermia during CPB, fluid balance (hemofiltration), and weaning from CPB; (2b) intraoperative laboratory data: minimum levels of Hct on CPB, maximum levels of lactate on CPB, and minimum and maximum levels of blood glucose (BG) on CPB; and (3b) intraoperative transfusion data: units of packed red blood cells (PRBC), platelets, and fresh-frozen plasma (FFP) used.

(c) Postoperative factors: (1c) Postoperative clinical characteristics: the presence of atrial fibrillation (AF) rhythm, use of invasive arterial blood pressure (IABP), electroshock therapy, development of acute kidney injury (AKI), need for hemodialysis, development of cerebral vascular accident (CVA), drainage data, red-cell storage time, sleep quality assessed by the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al. 1989), use of physical restraint, length of stay (LOS) in the ICU, and hospital length of stay; (2c) postoperative transfusion data: units of PRBC, platelets, and FFP used; (3c) postoperative environmental factors in the ICU: measurement of lux in the ICU involved measuring and evaluating the lighting conditions. The luximeter was placed in patients' rooms in the ICU and measured the light levels three times a day (morning, afternoon, evening); sound metrics measured by the TES 1352A sound level meter (SLM) device (TES Electrical Electronic Corp., Taiwan) with a range of 30–130 decibel (dB) (Sosa et al. 2018) (Sosa et al. 2018), temperature of ICU by thermometers, humidity of ICU by hygrometers, and bed position according to bed location, and patients were divided into two groups: the natural light (NL) group, consisting of patients positioned near a window, and the artificial light (AL) group, comprising patients positioned near the door or far from the window (Vahedian-Azimi et al. 2020); (4c) postoperative medication data: administration of midazolam, morphine, fentanyl drip, dexmedetomidine, dexamethasone, and norepinephrine; and (5c) postoperative laboratory data: sodium, potassium, Hct, and minimum and maximum levels of blood glucose and lactate.

Statistical analysis

Categorical variables were expressed as counts (percentage) and continuous variables as mean ± standard deviation (SD). Demographic and clinical characteristics were assessed using Student's *t*-test (normal distribution) or Mann–Whitney *U*-test (in the cases of skewed distribution) with continuous variable and chi-square or Fisher's exact test (as appropriate) with categorical variables. Chi-square automatic interaction detector (CHAID) decision tree analysis was used to identify risk factors for delirium after cardiac surgery. Delirium development was considered the dependent variable, while all pre-, intra-, and postoperative risk factors were treated as independent variables. The minimum parent and child nodes were determined as 100 and 50, respectively. "Nodes" are midpoints or

terminal points after bifurcation according to each factor. Based on the result, a group of patients was divided into one of the terminal nodes (risk groups) with calculated predictive probability.

Univariate and multivariate binary logistic regression estimated the influence of the variables on the relative likelihood of the delirium. In the univariate analysis, each variable was entered into separate models, and, subsequently, associated variables with $P<0.05$ were entered into a multivariate backward stepwise Wald model. The results of the regression analysis were presented as odds ratios (OR) with corresponding 95% confidence intervals (95% CI). To assess the predictive accuracy of risk factors in determining delirium, receiver operating characteristic (ROC) curves and the corresponding area under the curves (AUC) were calculated via the final multivariate model (based on the cumulative effect of four risk factors: hearing impairment history, addiction history, benzodiazepines, and sleep quality in first night after cardiac surgery). The AUC values were interpreted based on general guidelines: AUC between 0.9 and 1.0 indicated excellent discriminative power, 0.8–0.9 indicated good power, 0.7–0.8 indicated fair power, and 0.6–0.7 indicated poor power. Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and Youden index were also considered to determine appropriate cut-off points. An internal cross-validation in 1000 bootstrap samples was performed to further evaluate the predictive accuracy of the screening instrument. Calibration of the model was assessed and graphically displayed by plotting observed risk of postoperative delirium against predicted risk of delirium across 20% risk strata.

To examine the joint effects of poor quality of sleep at first night and having benzodiazepine history on delirium development, interactions with both multiplicative and additive scales were calculated. The effect of multiplicative interaction was calculated directly by odds from binary logistic regression model (de Mutsert et al. 2009; Kalilani and Atashili 2006). The relative excess risk due to interaction (RERI), and attributable proportion due to interaction (AP) and synthetic index (S), indicated the effect of additive interaction (AI) (Andersson et al. 2005), and $RERI \neq 0$, $AP \neq 0$, or $S \neq 1$ represent a biological AI, which was used in the previous study (Yang et al. 2012).

The statistical analysis was performed using Stata version 17 (Stata Corp., TX, USA, RRID: SCR_012763), SPSS software version 21 from SPSS Inc. (IL, Chicago, USA), GraphPad Prism 9© from GraphPad Software Inc. (La Jolla, CA, USA), and MedCalc software. A significance level of <0.05 was used for all analyses.

Results

Patient characteristics

The study included a total of 920 patients who underwent cardiac surgery. The mean ± SD age of patients was 59.43 ± 12.65 years, and the majority of patients were men (67.4%). All patients underwent coronary artery bypass grafting (CABG). Delirium was diagnosed in 488 (53%) of patients. In our analysis, a high level of agreement was observed between the assessors, as indicated by Cohen's kappa coefficient ($\kappa=0.94$, $P<0.001$).

Patients with delirium were older ($P<0.001$), had a lower education level ($P<0.001$), higher CCI score ($P<0.001$), higher EuroSCORE ($P<0.001$), and higher APACHE II score ($P<0.001$) (Table 1). Moreover, the intraoperative characteristics indicated that delirium was associated with higher grafts used ($P<0.001$), longer surgery duration ($P<0.001$), longer CPB duration ($P<0.001$), longer duration of aortic clamp usage ($P<0.001$), higher MAP during CPB ($P=0.030$), lower rate of ultrafiltration ($P<0.001$), and a higher requirement for PRBC blood products ($P<0.001$) (Table 2). In the postoperative period, delirium was also associated with the presence of AF rhythm ($P<0.001$), use of IABP ($P<0.001$), electroshock therapy ($P=0.025$), the need for hemodialysis ($P<0.001$), higher amount of drainage ($P<0.001$), poor sleep quality in the first ($P<0.001$) and second night after cardiac surgery ($P<0.001$), longer length of stay in ICU ($P<0.001$) and hospital ($P<0.001$), increased requirement for PRBC blood products ($P<0.001$), and higher lux measurement in the morning ($P<0.001$) (Table 3).

Delirium prediction based on CHAID results

The decision tree algorithm revealed six risk factors associated with delirium incidence: ICU — open heart (OH), length of stay (LOS), use of fentanyl drip, weaning from CPB, ambient noise level (sound metric), red-cell storage time, and severity of illness based on the APACHE II score (Fig. 1). Based on the observed data, the probability of delirium was 94% and 16.6% for patients with an ICU-OH LOS >4 and ≤ 3 days, respectively. When the total dosage of fentanyl drip exceeded 0.21 mg, the probability of delirium was as high as 96.9%, whereas it was 86.1% for dosages of 0.20 mg or less ($\chi^2=17.352$, $P<0.001$). In a sub-node analysis, the probability of delirium increased to 98.7% when the fentanyl drip dosage was >0.21 mg, and the ambient noise level was 52 dB or less. Conversely, the probability decreased to 92% when the ambient noise level was also 52 dB or more ($\chi^2=0.446$, $P=0.002$). Moreover, for patients with a fentanyl drip dosage ≤ 0.20 mg or less, the probability of delirium development was 96.4% for a red-cell storage time exceeding 18 days and 76.3% for a storage time ≤ 17 days or less ($\chi^2=0.747$, $P=0.002$).

Table 1 Comparison of preoperative risk factors in participants with and without delirium

Preoperative risk factors	Patients without delirium (*n* = 443)	Patients with delirium (*n* = 488)	*p*-value
Demographic characteristics			
Age in years, (mean ± SD)	52.94 ± 12.84	65.17 ± 9.26	< 0.001*
Male gender (%)	306 (70.8)	314 (64.3)	0.036*
Married patients (%)	388 (89.8)	478 (98)	< 0.001*
Having family support (%)	413 (95.6)	465 (95.3)	0.819
Body mass index, (mean ± SD)	26.17 ± 4.57	26.98 ± 11.60	0.175
Education level, diploma and higher (%)	339 (78.5)	182 (37.3)	< 0.001*
Smoker, yes (%)	73 (16.9)	236 (48.4)	< 0.001*
Addiction, yes (%)	17 (3.9)	121 (24.8)	< 0.001*
Clinical characteristics			
Charlson Comorbidity Index (CCI) score, ≥ 4 (%)	137 (31.7)	361 (74)	< 0.001*
APACHE II, ≤ 10 (%)	60 (13.9)	364 (74.6)	< 0.001*
EURO score, ≥ 3 (%)	123 (28.5)	355 (72.7)	< 0.001*
Metabolic syndrome, yes (%)	1 (0.2)	5 (1)	0.136
Ejection fraction (EF), ≤ 50% (%)	199 (46.1)	344 (70.5)	< 0.001*
Carotid status, **s**tenosis < 50% with occlusion (%)	319 (73.8)	210 (43)	< 0.001*
Nutrition status, malnourished (%)	1 (0.2)	1 (0.2)	0.931
Angiography history, ≥ 8 (%)	231 (53.5)	200 (41)	< 0.001*
Parkinson**'**s disease history, yes (%)	1 (0.2)	7 (1.4)	0.073
Sleep disorder history, yes (%)	60 (13.9)	362 (74.2)	< 0.001*
Psychiatric disorder history, yes (%)	2 (0.5)	31 (6.4)	< 0.001*
Speech problem history, yes (%)	1 (0.2)	7 (1.4)	0.073
Visual impairment history, yes (%)	40 (9.3)	192 (39.3)	< 0.001*
Hearing impairment history, yes (%)	11 (2.5)	133 (27.3)	< 0.001*
Admission history, yes (%)	260 (60.2)	445 (91.2)	< 0.001*
Coronary artery disease (CAD), yes (%)	292 (67.6)	315 (64.5)	0.331
Valve impairments, yes (%)	140 (32.4)	173 (35.5)	0.331
Laboratory data			
Hematocrit (Hct) levels, median (IQR)	43.3 (39.05–64.4)	40.5 (36.8–44.20)	< 0.001*
Creatinine (Cr) levels (mg/dL), median (IQR)	1.1 (0.9–1.2)	1.2 (1–1.3)	< 0.001*
Medication data			
Atorvastatin history, yes (%)	384 (88.9)	465 (95.3)	< 0.001*
Warfarin history, yes (%)	3 (0.7)	11 (2.3)	0.062
Benzodiazepines history, yes (%)	59 (13.7)	353 (72.3)	< 0.001*
Number of medications, ≥ 4 (%)	234 (54.2)	374 (76.6)	< 0.001*

* $P < 0.05$ was considered as significant

However, the probability of delirium was 55.7% when the ICU-OH LOS was ≤ 3 days and CPB weaning required external assistance ($\chi^2 = 90.051$, $P < 0.001$). In cases where CPB weaning was done without external assistance, the APACHE II score was checked. If the score was above 10, the probability of delirium was 32.8% ($\chi^2 = 38.293$, $P < 0.001$).

Delirium prediction using multivariate regression

Multivariate regression analysis revealed that 14 variables were associated with delirium as follows: older age (*OR*: 1.352, 95% *CI*: 1.022–2.082), chronic opioid use (*OR*: 6.895, 95% *CI*: 4.712–8.188), hearing impairment (*OR*: 4.711, 95% *CI*: 1.293–7.163), history of benzodiazepine use (*OR*: 5.406, 95% *CI*: 2.937–9.949), emergency cardiac surgery (*OR*: 3.872, 95% *CI*: 1.762–8.509), poor sleep quality on the first night after cardiac surgery (*OR*: 7.628, 95% *CI*: 4.470–9.015), higher amount of drainage (*OR*: 4.856, 95% *CI*: 2.837–8.315), longer red-cell storage time (*OR*: 2.801, 95% *CI*: 1.641–4.783), higher levels of lactate on the third day after surgery (*OR*: 6.319, 95% *CI*: 3.640–9.971), use of higher doses of midazolam (*OR*: 2.956, 95%

Table 2 Comparison of intraoperative risk factors in participants with and without delirium

Intraoperative risk factors	Patients without delirium (*n* = 443)	Patients with delirium (*n* = 488)	*p*-value
Clinical characteristics			
Grafts used, ≥ 3 (%)	204 (47.2)	316 (64.8)	< 0.001*
Second time surgery, yes (%)	17 (3.9)	22 (4.5)	0.667
Duration of surgery, ≥ 247 min (%)	147 (34)	326 (66.8)	< 0.001*
Cardiopulmonary bypass (CPB), yes (%)	415 (96.1)	486 (99.6)	0.956
CPB duration, ≥ 80 min (%)	159 (36.8)	307 (62.9)	< 0.001*
Duration of aortic clamp, ≥ 48 min (%)	177 (41)	299 (61.3)	< 0.001*
Main **a**rterial **p**ressure (MAP) during CPB, ≥ 72 (mmHg)	200 (46.3)	261 (53.5)	0.030*
PaO2 during CPB, ≥ 346 (mmHg)	215 (49.8)	256 (52.5)	0.415
Hypothermia during CPB, ≤ 32 °C (%)	166 (38.4)	261 (53.5)	< 0.001*
Hemofiltration, ≤ 2 **L**/h (%)	155 (35.9)	256 (52.5)	< 0.001*
CPB weaning, with external helping (%)	43 (10)	352 (66.6)	< 0.001*
Laboratory data			
Minimum hematocrit level on CPB, median (IQR)	25 (22–26)	22 (20–25)	< 0.001*
Maximum lactate on CPB (mmol/L), median (IQR)	1.4 (1.2–1.8)	1.8 (1.4–2.4)	< 0.001*
Minimum blood glucose during CPB (mg/dL), median (IQR)	124 (88–146)	136 (98–165)	< 0.001*
Maximum blood glucose during CPB (mg/dL), median (IQR)	166 (143–198)	198 (166.25–248.75)	< 0.001*
Blood transfusion data			
Blood product, packed red blood cells (PRBC)	142 (32.9)	277 (56.8)	< 0.001*
Blood product, platelets	290 (67.1)	211 (43.2)	

* $P < 0.05$ was considered as significant

CI: 1.751–4.989), and fentanyl drip (*OR*: 3.519, 95% *CI*: 2.045–6.053); higher education level (*OR*: 0.307, 95% *CI*: 0.171–0.549), higher ambient noise level in the morning (sound metric) (*OR*: 0.387, 95% *CI*: 0.165–0.909), and higher doses of dexamethasone (*OR*: 0.260, 95% *CI*: 0.140–0.483) were significantly associated with a lower risk of delirium.

Ten variables were subsequently excluded from the model as their inclusion only marginally improved AUC by less than one percentage point and were not deemed essential from a clinical perspective. The final model, as depicted in Fig. 2, comprised four predictors: chronic opioid use (*OR*: 4.605, 95% *CI*: 2.163–9.804), hearing impairment (*OR*: 6.926, 95% *CI*: 3.630–12.215), benzodiazepine history (*OR*: 8.506, 95% *CI*: 5.651–11.805), and poor sleep quality on the first night after cardiac surgery (*OR*: 9.081, 95% *CI*: 6.225–12.248). The contribution of each variable to the predictive screening instrument was determined based on its regression coefficient. For ease of use, these coefficients were multiplied by 30 and referred to as "risk scores" (Fig. 2). For instance, a patient with a history of benzodiazepine uses and poor sleep quality on the first night after surgery would have a total risk score of 64.2 + 66 = 130.2. This total risk score can be plotted on a risk probability curve. The resulting predictive screening instrument is illustrated in Fig. 3.

A ROC curve analysis conducted to predict delirium based on the cumulative effect of four variables in the final model revealed an AUC of 0.897 (95% *CI*: 0.876–0.916), indicating a good power predictive ability (Fig. 4). The *P*-value was < 0.0001, indicating statistical significance, with the standard error 0.0100. The sensitivity was 70.7% (95% *CI*: 66.4–74.7), while the specificity (SP) was 91.9% (95% *CI*: 88.9–94.3). The positive likelihood ratio was 8.73 (95% *CI*: 6.32–12.05), and the negative likelihood ratio was 0.32 (95% *CI*: 0.28–0.37). The Youden index was 0.625. The suggested cut point for predicting delirium was > 0.48991 (Table 4). Figure 5 displays the relationship between observed and predicted risk of delirium development across four risk strata.

The interactions between poor sleep quality and having benzodiazepine history on delirium development

Table 4 shows the interactions of poor sleep quality at the first night and benzodiazepine history on delirium development, in the binary logistic regression model. The multiplicative interaction and additive interaction were statistically significant (*P*-value < 0.05). The delirium development in individuals with poor sleep quality at the first night and benzodiazepine history was 71.47 times higher than that of individuals without these two risk factors. Moreover, 70% of the risk of delirium

Table 3 Comparison of postoperative risk factors in participants with and without delirium

Postoperative risk factors	Patients without delirium ($n=443$)	Patients with delirium ($n=488$)	*p*-value
Clinical characteristics			
The presence of atrial fibrillation (AF) rhythm, yes (%)	8 (1.9)	55 (11.3)	< 0.001*
Use of invasive arterial blood pressure (IABP), yes (%)	2 (0.5)	46 (9.4)	< 0.001*
Electroshock therapy, yes (%)	2 (0.5)	11 (2.3)	0.025*
Acute tubular necrosis (ATN), yes (%)	22 (5.1)	241 (49.4)	< 0.001*
Need for hemodialysis, yes (%)	2 (0.5)	72 (14.8)	< 0.001*
Cerebral vascular accident (CVA), yes (%)	2 (0.5)	2 (0.4)	0.903
Drainage data, median (IQR)	240 (180–320)	450 (320–660)	< 0.001*
Red-**c**ell storage time, median (IQR)	0.001 (0.001–12)	18 (15–20)	< 0.001*
Sleep quality in first night after surgery, ≤ 270	97 (22.5)	378 (77.5)	< 0.001*
Sleep quality in second night after surgery, ≤ 240	37 (8.6)	201 (41.2)	< 0.001*
Use of physical restraint, yes (%)	423 (97.9)	478 (98)	0.971
ICU-OH length of stay, ≥ 4 days	26 (6)	407 (83.4)	< 0.001*
Hospital length of stay, ≥ 9 days	50 (11.6)	393 (80.5)	< 0.001*
Blood transfusion data			
Blood product, packed red blood cells (PRBC)	42 (9.7)	266 (54.5)	< 0.001*
Blood product, platelets	390 (90.3)	222 (45.5)	
Environmental factors			
Lux measurement in the morning, ≥ 54 (%)	368 (85.2)	390 (79.9)	0.036*
Lux measurement in the evening, ≥ 260 (%)	409 (94.7)	456 (93.4)	0.431
Lux measurement in the night, ≥ 271 (%)	358 (82.9)	415 (85)	0.370
Sound metrics in the morning, ≥ 41 (dB)	29 (6.7)	38 (7.8)	0.532
Sound metrics in the evening, ≥ 65 (dB)	111 (25.7)	153 (31.4)	0.058
Sound metrics in the night, ≥ 53 (dB)	90 (20.8)	124 (25.4)	0.101
Temperature, ≥ 27 ℃	260 (60.2)	311 (63.7)	0.269
Humidity, ≥ 11%	284 (65.7)	322 (66)	0.938
Bed position, natural light (NL) group, near to window	239 (55.3)	229 (46.9)	0.011*
Medication data			
Midazolam, ≥ 7 (%)	103 (23.8)	331 (67.8)	< 0.001*
Morphine, ≥ 9 (%)	72 (16.7)	213 (43.6)	< 0.001*
Fentanyl drip, ≥ 0.21 (%)	188 (43.5)	358 (73.4)	< 0.001*
Dexmedetomidine, ≥ 400 (%)	288 (66.7)	275 (56.4)	0.001*
Dexamethasone, ≥ 9 (%)	145 (33.6)	128 (26.2)	0.015*
Norepinephrine, ≥ 1 (%)	5 (1.2)	110 (22.5)	< 0.001*
Laboratory data			
Sodium levels in first day, ≥ 140 (mEq/L)	235 (54.4)	260 (53.3)	0.734
Sodium levels in second day, ≥ 140 (mEq/L)	196 (45.4)	255 (52.3)	0.037*
Sodium levels in third day, ≥ 140 (mEq/L)	219 (50.7)	254 (52)	0.692
Potassium levels in first day, ≥ 4.21 (mEq/L)	191 (44.2)	256 (52.5)	0.013*
Potassium levels in second day, ≥ 4.21 (mEq/L)	185 (42.8)	276 (56.6)	< 0.001*
Potassium levels in third day, ≥ 4.21 (mEq/L)	201 (46.5)	291 (59.6)	< 0.001*
Hematocrit levels in first day, ≥ 26.11	282 (65.3)	171 (35)	< 0.001*
Hematocrit levels in second day, ≥ 27.61	283 (65.5)	182 (37.3)	< 0.001*
Hematocrit levels in third day, ≥ 29.21	282 (65.3)	186 (38.1)	< 0.001*
Minimum blood glucose in first day, ≤ 175 (mg/dL)	270 (62.5)	186 (38.1)	< 0.001*
Maximum blood glucose in first day, ≥ 242 (mg/dL)	164 (38)	312 (63.9)	< 0.001*
Minimum blood glucose in second day, ≤ 155 (mg/dL)	264 (61.1)	194 (39.8)	< 0.001*
Maximum blood glucose in second day, ≥217 (mg/dL)	152 (35.2)	309 (63.3)	<0.001*
Minimum blood glucose in third day, ≤133 (mg/dL)	246 (56.9)	211 (43.2)	<0.001*
Maximum blood glucose in third day, ≥176 (mg/dL)	161 (37.3)	304 (62.3)	<0.001*
Lactate levels in first day, ≥4.71 (mmol/L)	129 (29.9)	331 (67.8)	<0.001*
Lactate levels in second day, ≥3.1 (mmol/L)	136 (31.5)	343 (70.3)	<0.001
Lactate levels in third day, ≥1.41 (mmol/L)	117 (27.1)	332 (68)	<0.001*

* $P<0.05$ was considered as significant

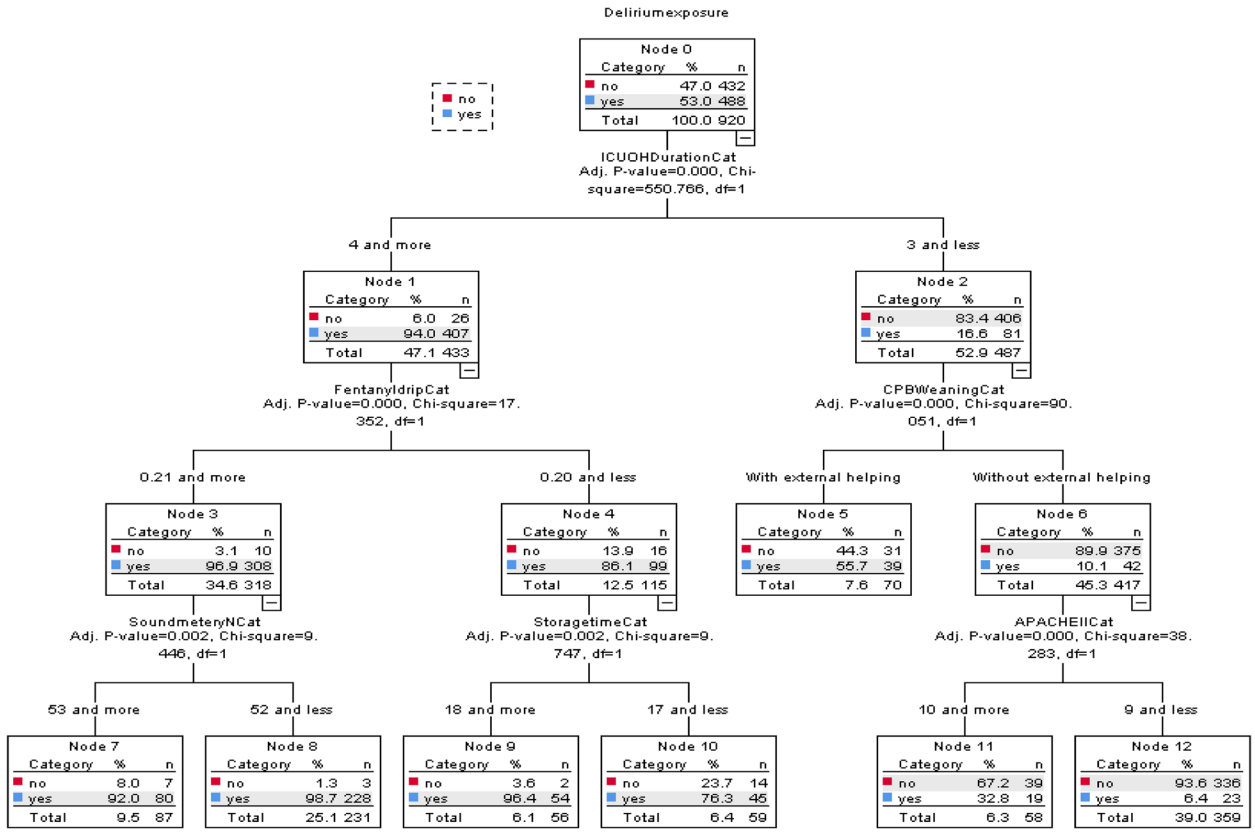

Fig. 1 A chi-square automatic interaction detector (CHAID) decision classification tree analysis to predict delirium incidence

Risk factors	Univariate OR (95%CI), P-value	Multivariate OR (95%CI), P-value	Multivariate OR to predict delirium incidence	Regression coefficient	Risk score
Opium addiction	8.049 (4.753-12.629), 0.001	4.605 (2.163-9.804), 0.001		1.52	45.6
hearing impairment	4.339 (2.631-8.947), 0.001	6.926 (3.630-12.215), 0.001		1.93	57.3
history of benzodiazepine use	6.531 (3.781-10.196), 0.001	8.506 (5.651-11.805), 0.001		2.14	64.2
Poor sleep quality	7.868 (5.704-11.182), 0.001	9.081 (6.225-12.248), 0.001		2.20	66

Fig. 2 Univariate and multivariate binary logistic regression to predict delirium after cardiac surgery according to risk factors that entered to finale model for developing screening tool. Abbreviation: OR, odds ratio; CI, confidence interval

was attributable to the interaction between these two exposures.

Discussion

In this multicenter, multiphase study, we evaluated potential risk factors associated with the development of delirium after cardiac surgery and utilized this information to develop the novel SDACS screening tool for early postoperative prediction of delirium. Based on the findings of this study, the prevalence of delirium after cardiac surgery is high (53%) and depends on chronic opioid use, hearing impairment, benzodiazepine use, and poor sleep quality on the first night after cardiac surgery. The incidence of delirium in our report was higher compared to other studies (Andrási et al., 2022; Ordóñez-Velasco and Hernández-Leiva 2021) and consistent with the others (Chen et al. 2021; Smulter et al. 2013). Of note is that the observation period for delirium in our study was longer than in most of the available studies in literature, extending up to the third postoperative day.

The CHAID decision tree analysis revealed several factors associated with the development of delirium, including ICU length of stay ≥ 4 days, use of fentanyl drip, ambient noise levels, red-cell storage time ≥ 18 days,

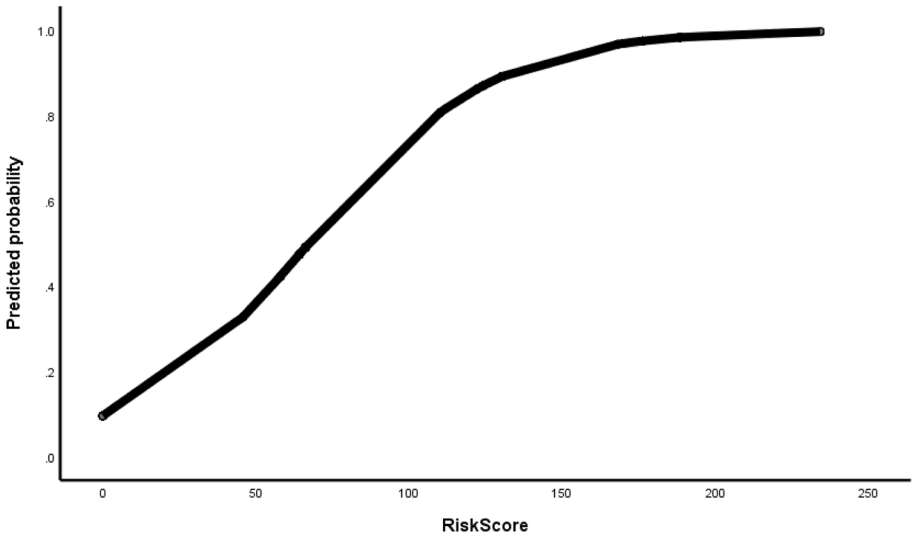

Fig. 3 The predictive screening instrument; the plot showed the total risk score, obtained from the screening tool, on the curve and estimate the corresponding risk for delirium after cardiac surgery

CPB weaning with external assistance, and APACHE II score > 10. Indeed, prolonged ICU stays can disrupt sleep and expose patients to stressors, thereby increasing the risk of delirium (Showler et al. 2023), while the constant noise and bright lights in the ICU environment can also contribute to sleep disturbances (Karimi et al. 2021). Additionally, patients with longer ICU stays often undergo more medical interventions, which can directly impact the risk of delirium (Vahedian Azimi et al. 2015). One of these medical interventions is fentanyl drip, a potent opioid analgesic, which may contribute to delirium development due to its sedative effects and potential for respiratory depression (Casamento et al. 2023; Casault et al. 2021).

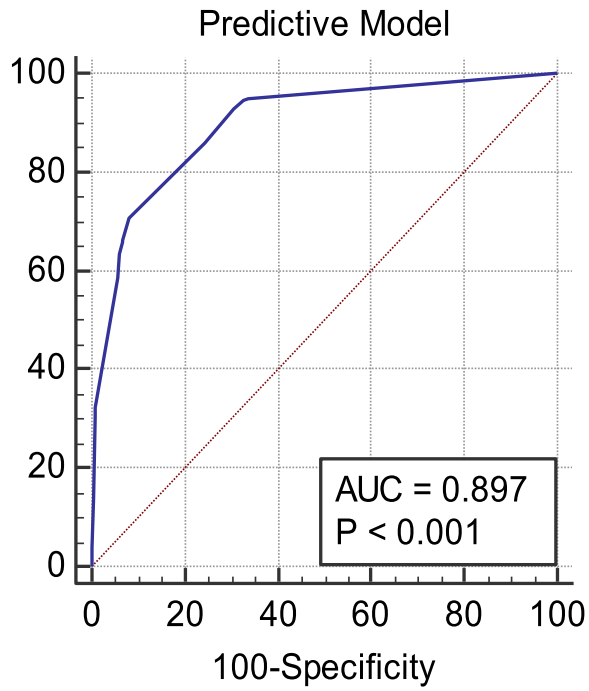

Fig. 4 Area under the receiver operating curve of the predictive model to early detection delirium after cardiac surgery

In addition, previous research indicates that red-cell storage beyond 14 or 21 days increases the risk of delirium after cardiac surgery (Casault et al. 2021). This is likely due to changes in red blood cells, such as decreased pH, degradation of 2,3-disphosphoglycerate, hindered oxygen release, and reduced ability to induce vasodilation and enhance oxygen delivery, which can impair the physiology and function of the nervous system (Maldonado 2008; Zubair 2010). During CPB weaning, factors such as anesthesia, inflammation, hemodynamic instability, and cerebral blood flow alterations can also contribute to delirium development (Faisal et al. 2023). Weaning with external assistance and overtreatment may lead to dysregulated cerebral blood flow and hyperperfusion, and potential brain dysfunction, thereby increasing the risk of delirium. Cardiac surgery patients with high postoperative APACHE II scores may experience physiological derangements and organ dysfunction, which can contribute to the development of delirium (Lin et al. 2020; Wang et al. 2023).

In the present study, multivariate regression analysis identified several risk factors, with older age being a significant non-modifiable one. The increased incidence of delirium in elderly patients can be attributed to

Table 4 Interactions between poor quality of sleep on the first night after surgery and having benzodiazepine history on delirium incidence

Additive interaction			Multiplicative interaction	Interaction
S (95% *CI*)	**AP (95% *CI*)**	**RERI (95% *CI*)**	**HR (95% *CI*)**	
3.43 (1.51–5.35)	0.70 (0.54–0.86)	71.47 (14.09–128.85)	22.32 (14.25–34.96)	Sleep and benzodiazepine

Abbreviations: *HR* hazard ratio, *RERI* relative excess risk due to interaction, *AP* attributable proportion, *S* synthetic index

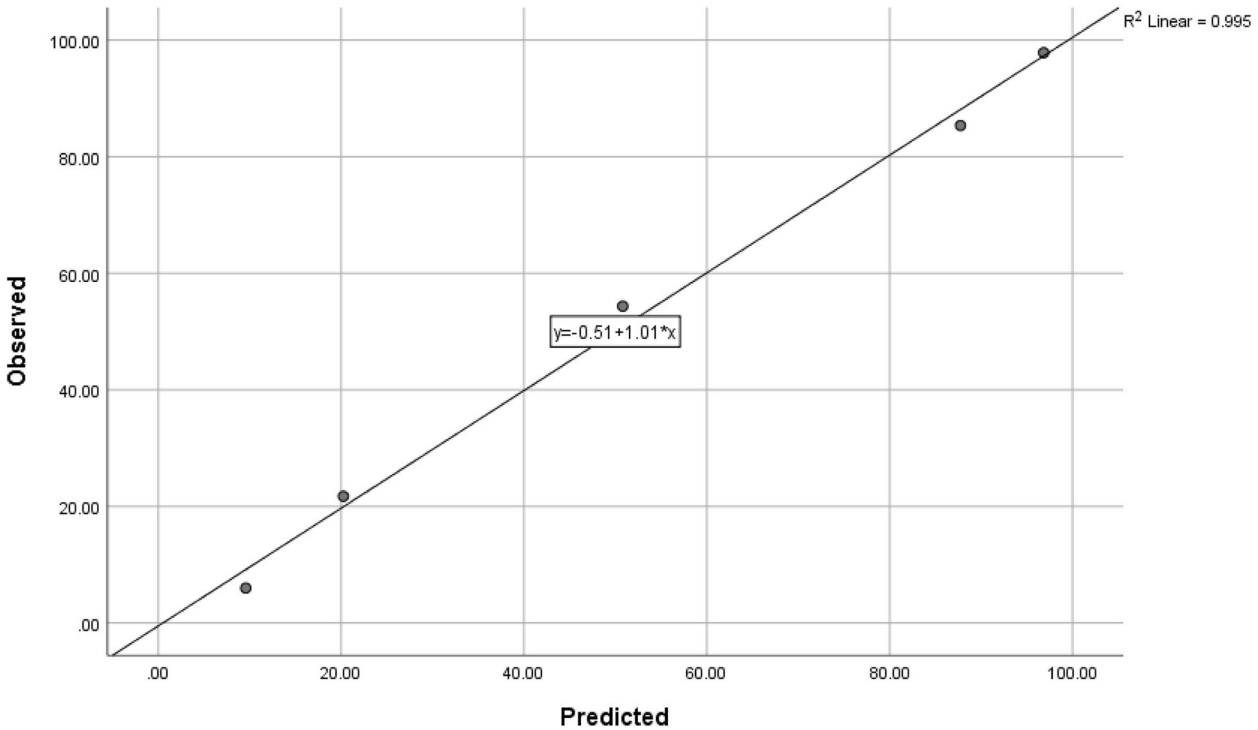

Fig. 5 Calibration curve comparing observed and predicted risk of delirium after cardiac surgery across 20% strata

age-related physiological changes, such as alterations in neurotransmitter systems, decreased cerebral blood flow, and heightened susceptibility to inflammation, which can compromise cognitive function (Bugiani 2021). Additionally, multiple comorbidities and polypharmacy worsen cognitive impairment and increase vulnerability to delirium (Kotfis et al. 2018). Reduced cognitive reserve and impaired processing in the elderly, combined with the stressors of surgery or hospitalization, can further overwhelm their cognitive capacity (Tow et al. 2016). We also found a significant association between higher education level and a decreased risk of delirium. This finding aligns with previous studies suggesting that education levels may impact cognitive reserve and function (Ordóñez-Velasco and Hernández-Leiva 2021; Xue et al. 2020).

We also observed significant associations between various postoperative factors and the development of delirium. These factors include a higher amount of drainage, longer red-cell storage time, elevated ambient noise levels in the ICU, higher levels of lactate on the third day after surgery, higher dose of dexamethasone, and use of higher doses of midazolam, and fentanyl drip confirms findings that align with previous research. The only environmental factor that had a statistically significant effect on the odds of delirium incidence was the morning elevated ambient noise levels, which were negatively associated with delirium. This suggests that increasing ambient noise in the ICU from 8 am to 12 pm could be protective against delirium, which is consistent with the findings of a previous study (Sangari et al. 2021). This finding raises interesting considerations regarding the importance of maintaining sleep/wake cycles in the ICU. Care teams that prioritize patient participation in morning care goals and aim to awaken patients in the morning may

inadvertently contribute to higher ambient noise levels during that time. Interventions such as "opening the curtains" to increase light in the room are often employed to initiate the day. However, our results indicate that the morning light average did not have a significant effect on the incidence of delirium. The evening and night sound averages did not show statistically significant effects on the odds of delirium incidence. This finding is crucial as it emphasizes the notion that preventing delirium may not require major changes. Instead, delirium prevention may rely on making small, targeted modifications to clinical behavior and the environment (Marra et al. 2017).

Of note, poor quality sleep on the first night after surgery was identified in our study as one of the strongest factors associated with the development of delirium (*OR*: 9.081) (Evans et al. 2017; He et al. 2022; Wang et al. 2021). The link between poor sleep and delirium can be attributed to various factors including environmental-related ICU factors, such as artificial light, ambient noise, and alarms from monitoring devices, and patient-related factors like pain, stress, increased inflammation, and alterations in neurotransmitter levels (Karimi et al. 2021). The exact mechanism is unclear, but, as stated previously, factors like neuroinflammation, oxidative stress, and altered brain function may be associated with delirium after cardiac surgery in individuals with postoperative sleep disturbance (Wang et al. 2021). In addition, benzodiazepine use, hearing impairment, and addiction can contribute to the occurrence of delirium due to their effects on the central nervous system.

Critical care nurses are in the best position to detect and monitor delirium in critically ill patients. Therefore, an optimum delirium assessment tool with strong evidence should be identified with critical care nurses to perform in the daily assessment (Agarwal et al., 2020). It is worth mentioning that the optimal method for assessing postoperative delirium following surgery has yet to reach a generalized consensus. A comparison of methods in the ICU found the confusion assessment method for the ICU (CAM-ICU) demonstrated higher diagnostic test accuracy and is recommended as the optimal delirium assessment tool (Agarwal et al., 2020; Devlin et al., 2018). However, using this test is time-consuming, especially for providers not formally trained to complete the assessment.

Another prospective, international multicenter study assessed the E-PRE-DELIRIC, also consisting of many predictors assessed at ICU admission (Wassenaar et al. 2015). In contrast, the SDACS use only four, easy-to-assess, independent predictors, i.e., chronic opioid use, history of hearing impairment, benzodiazepine use, and postoperative poor-quality sleep, and has an AUC of 0.897, indicating an almost excellent discriminative power. Furthermore, each of the aforementioned predictors contributes a specific risk score, as illustrated in Fig. 2. These individual risk scores are then summed up to calculate a total risk score. By triaging patients based on their risk estimation, resources can be allocated effectively for the early prediction of delirium. For example, our method may emphasize the significance of addressing sleep disturbances and implementing strategies to improve sleep quality after cardiac surgery, which can help reduce the occurrence and severity of delirium. It is worth noting that the SDACS screening instrument differs from the "short clinical assessment" and "functional assessment" described in the NICE guidelines in that it provides a risk estimation as a percentage, which can be valuable in clinical practice.

Strengths and limitations

Important strengths of this study include the use of a large cohort, the prospective data collection, and its multicenter, multiphase design including a comprehensive scoping review of published papers, the involvement of three Delphi rounds to identify multiple potential predictors of delirium, patients from three academic hospitals, a rigorous statistical methodology, and the development of the SDACS screening tool with good predictive power. In addition, we considered clinically relevant variables that are known to play a significant role in the development of postoperative delirium. The higher prevalence of postoperative delirium in our study also demonstrates a comprehensive and accurate delirium assessment performed by trained nurses and researchers, with a high level of kappa agreement. Another strength is that standard institutional protocols were followed for preoperative evaluation, premedication, and anesthetic and surgical procedures, without any modifications, increasing the pragmatism of the study. However, we acknowledge some limitations. Given the observational nature of this study, the findings should be validated in a randomized controlled trial setting. The study did not include external validation of the screening tool, highlighting the need for further research to confirm its effectiveness in other patient populations. Convenience sampling technique may have also introduced some selection bias and would be an additional point to be made here alongside the observational nature of the study. However, the multicenter design of the present study enhances the applicability of the SDACS tool. Finally, differences in enrollment across centers may raise the risk of selection bias.

Conclusions

Chronic opioid use, history of hearing impairment, benzodiazepine use, and poor sleep quality on the first night after surgery are associated with delirium after cardiac surgery. The novel SDACS screening tool was effective in the early prediction of postoperative delirium in patients from three academic institutions. Its ease of use, predictive power, sensitivity, and specificity favor its application in cardiac surgery patients. External validation is necessary before implementing this tool in other clinical settings and populations.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13741-025-00518-8.

Supplementary Material 1

Supplementary Material 2

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Authors' contributions
Hosein Mahmoudi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing-original draft, Writing—review & editing. Athanasios Chalkias: Conceptualization, Methodology, Software, Validation, Visualization, Writing—review & editing. Ali Moradi: Data curation, Formal analysis, Visualization, Validation, Writing—review & editing. Seyed Tayeb Moradian: Data curation, Formal analysis, Validation, Writing—review &editing. Seyed Mohammad Reza Amouzegar: Data Curation, Formal analysis, Validation, Visualization, Writing—review & editing. Amir Vahedian-Azimi: Supervision, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Writing—review & editing.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was conducted in strict adherence to the principles of the Declaration of Helsinki and received approval from the Research Ethics Committees of Baqiyatallah University of Medical Sciences, Tehran, Iran (IR.BMSU.BAQ.REC.1400.052). Informed consent was obtained from all patients or their relatives, and the study findings were reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Nursing Care Research Center, Clinical Sciences Institute, Nursing Faculty, Baqiyatallah University of Medical Sciences, Tehran, Iran. [2]Institute for Translational Medicine and Therapeutics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA. [3]Outcomes Research Consortium, Cleveland, OH 44195, USA. [4]Atherosclerosis Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

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