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Evaluation of Intraoperative Cerebral Desaturation and Risk Factors Associated With Cognitive Dysfunction After Cardiac Surgery: A Prospective Observational Study

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Abstract

Background: Postoperative cognitive dysfunction (POCD) remains a common neurological complication after cardiac surgery, particularly among older patients. Intraoperative cerebral oxygen desaturation during cardiopulmonary bypass (CPB) may reflect impaired cerebral perfusion and is proposed as a contributing factor to postoperative cognitive impairment. This study aimed to evaluate the association between intraoperative cerebral oxygen desaturation and postoperative cognitive outcomes in patients undergoing cardiac CPB surgery. **Methods:** In this prospective observational study, 74 patients undergoing elective cardiac surgery with CPB between March 2023 and March 2024 were included. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) preoperatively and on postoperative days (PODs) 4, 7, and 30. Bilateral frontal regional cerebral oxygen saturation (rSO₂) was continuously monitored intraoperatively using near-infrared spectroscopy (NIRS). Cerebral desaturation was defined as a reduction of >20% in rSO₂ from baseline. A standardized intervention protocol was applied when this threshold was exceeded. **Results:** The incidence of POCD was 32.4% during the first postoperative week and decreased to 20.2% by POD 30. Patients who developed POCD were significantly older than those without POCD (median (interquartile range [IQR]): 63 [58–68] vs. 59 [52–65] years; $p = 0.026$). Intensive care unit (ICU) and total hospital stays were significantly longer in the POCD group (median ICU stay: 74 [51.3–96] vs. 50 [46–60] hours; $p < 0.001$; median hospital stay: 9 [8–15.5] vs. 7 [7–9] days; $p < 0.001$). Intraoperative rSO₂ values were significantly lower in the POCD group following the initiation of CPB, particularly during the hypothermic and rewarming phases (T2–T4). Percentage decreases in rSO₂ at T2, T3, and T4 showed significant positive correlations with MMSE scores on POD 4 ($r = 0.283, p = 0.014$; $r = 0.312, p = 0.007$; $r = 0.312, p = 0.007$, respectively) and POD 30 ($r = 0.314, p = 0.006$; $r = 0.270, p = 0.020$; $r = 0.349, p = 0.002$, respectively). **Conclusions:** Intraoperative cerebral oxygen desaturation during CPB, particularly during the initiation, hypothermic, and rewarming phases, was associated with decreased early and late-postoperative cognitive performance after cardiac surgery. Continuous intraoperative cerebral oxygenation monitoring using NIRS may enable earlier identification of cerebral hypoperfusion and facilitate timely interventions in patients at increased risk of POCD. **Clinical Trial Registration:** NCT07361068. <https://clinicaltrials.gov/search?term=NCT07361068>.

Keywords: cardiac surgery; postoperative cognitive dysfunction; neuropsychological test; Mini-Mental State Examination; near-infrared spectroscopy; cardiopulmonary bypass; cerebral oxygen saturation

1. Introduction

Patients undergoing cardiac surgery are particularly prone to postoperative neurological complications due to aging and the increasing prevalence of comorbidities. In addition to existing cardiovascular diseases, age-related frailty, reduced adaptive mechanisms, intraoperative neuroinflammation, and heightened susceptibility to hypoxemia further contribute to this risk [1]. Postoperative cognitive dysfunction (POCD) has been reported to affect a substantial proportion of cardiac surgery patients and has been associated with prolonged hospitalization, reduced survival, increased healthcare costs, and decreased quality of life [2].

The pathophysiology of POCD in surgeries involving cardiopulmonary bypass (CPB) has not yet been fully elucidated. However, current evidence supports a multifactorial etiology in which surgery-related, anesthesia-related, and patient-related factors interact through interdependent mechanisms. Impaired cerebral autoregulation, neuronal injury secondary to hypoperfusion, and microembolic phenomena have been proposed as key contributors to postoperative cognitive impairment [3]. In addition, a recent study by Glumac *et al.* [4] demonstrated that the systemic inflammatory response triggered by surgical trauma plays a role in the development of POCD and that preoperative corticosteroid administration was associated with a reduced in-



idence and severity of POCD. Hemodynamic changes induced by CPB may further adversely affect the microcirculation, thereby contributing to a reduction in cerebral perfusion. Risk factors for POCD include preoperative variables such as age, hypertension, diabetes, and educational level, as well as intraoperative and postoperative factors, including the type of surgery, CPB, and aortic cross-clamp duration, and postoperative atrial fibrillation [5,6]. In addition, Yan *et al.* [7] emphasized the critical role of cerebral hypoperfusion, neuroinflammatory processes, and intraoperative neuromonitoring strategies in the multifactorial etiology of POCD.

Near-infrared spectroscopy (NIRS) enables noninvasive measurement of cerebral oxygen saturation, allowing real-time monitoring of intraoperative hemodynamic changes and detection of clinically significant desaturation events. Regional cerebral oxygen saturation (rSO₂) values obtained by NIRS reflect the balance between cerebral oxygen supply and demand [8]. Previous studies have demonstrated that intraoperative cerebral oxygen desaturation may be associated with postoperative cognitive impairment [9–11].

Based on these considerations, we hypothesized that intraoperative cerebral oxygen desaturation during CPB is associated with decreased postoperative cognitive performance in patients undergoing cardiac surgery. Therefore, the present study aims to evaluate the relationship between intraoperative cerebral oxygen desaturation and POCD in order to explore perioperative factors that may be associated with postoperative cognitive outcomes.

2. Materials and Methods

2.1 Study Design and Ethical Approval

This prospective observational study was conducted between March 2023 and March 2024 at the Department of Anesthesiology and Reanimation, University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital. The study protocol was approved by the institutional ethics committee on February 22, 2023 (approval no: 011-KAEK-25 2023/02-15). Written informed consent was obtained from all participants before enrollment.

2.2 Patient Population and Grouping

A total of 102 patients scheduled for planned elective cardiac surgery with CPB were screened for eligibility. Inclusion criteria were: age ≥ 18 years, planned elective cardiac surgery with CPB, provision of written informed consent, absence of communication barriers that could interfere with preoperative and postoperative Mini-Mental State Examination (MMSE) assessment, no history of cerebrovascular disease, preoperative MMSE score ≥ 24 , education level of at least high school, and absence of any frontal deformity that could hinder NIRS monitoring. Eligible surgical procedures included isolated CABG, valve surgery (only), combined CABG and valve surgery, and aortic surgery. A cutoff value of 23/24 on the MMSE test

was accepted as the standard threshold commonly used for identifying cognitive impairment [12]. Exclusion criteria included preoperative use of antipsychotic or antidepressant medications, emergency cardiac surgery, presence of $\geq 50\%$ carotid artery stenosis, and age under 18 years, as well as prolonged postoperative mechanical ventilation or the need for extended postoperative sedation that precluded reliable cognitive assessment. In addition, patients who developed clinically evident postoperative delirium, as well as those diagnosed with postoperative delirium through routine clinical examination by the intensive care team, were excluded from the study.

Patients meeting the inclusion criteria and providing informed consent were divided into two groups according to their postoperative cognitive outcomes. Group 1 (POCD group) included patients whose MMSE scores dropped to ≤ 23 at any time during the postoperative assessment, whereas Group 2 (non-POCD group) consisted of patients whose MMSE scores remained ≥ 24 throughout all assessments. The patient selection process and distribution of the groups are summarized in Fig. 1.

2.3 Study Protocol

Eligible and consenting patients were evaluated during the preoperative anesthesia assessment. Demographic data, comorbidities, EuroSCORE risk evaluation, and current medications were recorded. The MMSE was administered preoperatively. Before the induction of anesthesia, bilateral NIRS probes were placed on the forehead, and baseline rSO₂ values were recorded. During surgery, invasive arterial pressure, electrocardiography, pulse oximetry, central venous pressure, arterial blood gas analyses, body temperature, transfused blood and blood products, aortic cross-clamp (ACC) and CPB times, and total operative time were recorded. In the postoperative period, the duration of mechanical ventilation, complications, and length of stay in the intensive care unit (ICU) were monitored.

Cognitive assessments were performed preoperatively and on postoperative days (POD) 4, 7, and 30. An MMSE score of ≤ 23 at any assessment point was defined as the presence of POCD [12]. All tests were administered by two independent anesthesiologists blinded to the study data. The primary endpoint of the study was the development of POCD, defined as a decrease in MMSE score to ≤ 23 at any postoperative measurement. Secondary endpoints included the relationship between intraoperative rSO₂ values and desaturation depth with postoperative cognitive outcomes, as well as the association of intraoperative parameters (CPB time, ACC time, and extubation time) and ICU/hospital length of stay with the occurrence of POCD.

2.4 Anesthesia and Perfusion Management

All patients underwent standard anesthesia induction with midazolam (Zolamid, Vem Pharmaceuticals, Istanbul, Türkiye) at 0.05–0.1 mg/kg, propofol (Propofol Fresenius, Bad Homburg, Germany) at 2 mg/kg, fentanyl

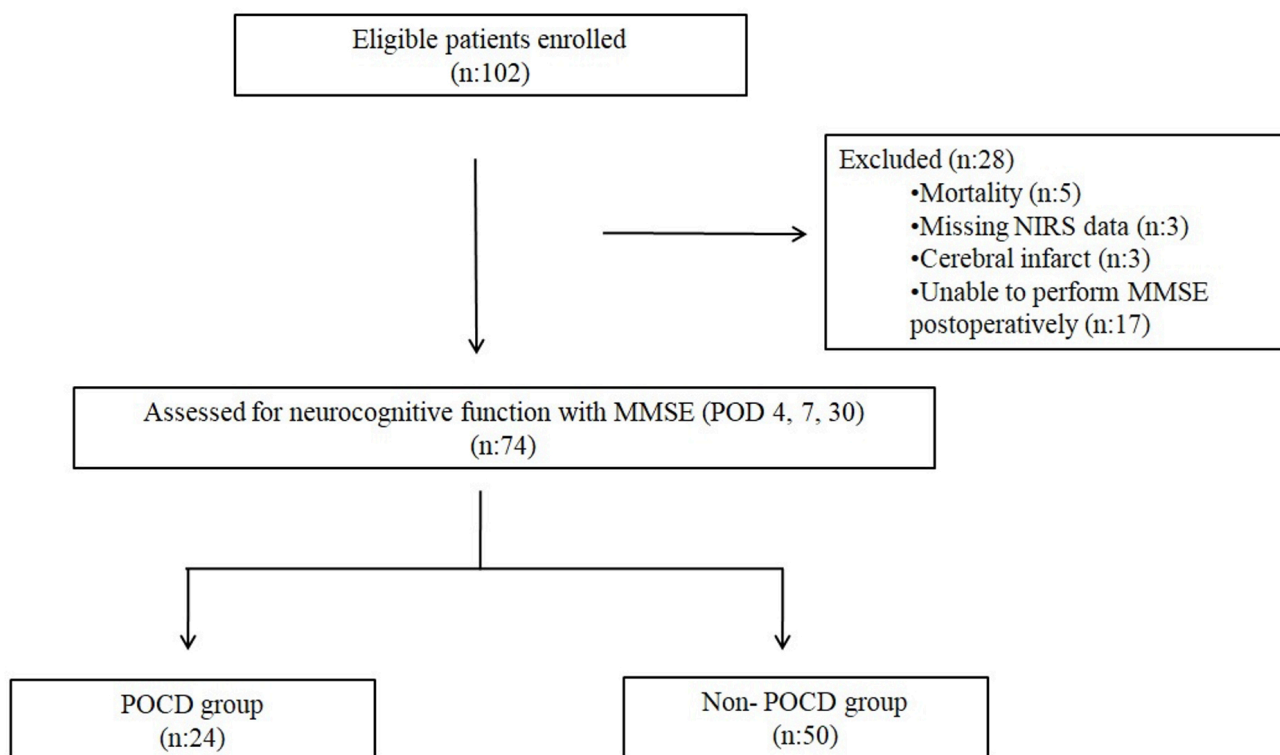


Fig. 1. Flow diagram of patient enrollment, exclusion, and study grouping. n, Number of patients; NIRS, Near-Infrared Spectroscopy; POD, Postoperative day; MMSE, Mini-Mental State Examination; POCD, Postoperative cognitive dysfunction.

(Talinat, Vem Pharmaceuticals, Istanbul, Türkiye) at 1–2 $\mu\text{g}/\text{kg}$, and rocuronium (Myokron, Vem Pharmaceuticals, Istanbul, Türkiye) at 0.6 mg/kg . An additional dose of fentanyl (3 $\mu\text{g}/\text{kg}$) was administered before sternotomy. Heparin (Koparin, Koçak Farma, Istanbul, Türkiye) was given before cannulation at a dose of 300–400 U/kg, and the activated clotting time was maintained above 400 seconds throughout CPB. Anesthesia was maintained with 2% sevoflurane, fentanyl, midazolam, and rocuronium in a mixture of 50% oxygen and 50% air. During CPB, perfusion flow was adjusted to 2.1–2.6 $\text{L}/\text{min}/\text{m}^2$, maintaining a mean arterial pressure between 50 and 70 mmHg. Arterial blood gas analyses were performed every 30 minutes, and hematocrit levels were kept above 20%. At the end of CPB, heparin was reversed with protamine sulfate. All patients were transferred to the ICU while still intubated.

In the postoperative ICU period, routine sedation was not administered to patients undergoing planned elective cardiac surgery. Once the effects of intraoperative anesthetic agents had resolved, the weaning process from mechanical ventilation was initiated. Sedative agents were administered only to patients who experienced difficulty with weaning or developed clinical indications such as respiratory or hemodynamic instability. These patients were excluded from the study.

2.5 Cerebral Oxygen Saturation Monitoring

Regional cerebral oxygen saturation values were measured using the INVOS™ 5100C monitor (Medtronic, Min-

neapolis, MN, USA) with two probes placed on the patient's frontal region. For data analysis, rSO_2 values obtained from the right and left frontal sensors were averaged, and a single cerebral oxygen saturation value was analyzed at each measured time point [13]. Measurements were recorded at the following time points: T0 (before induction), T1 (15 minutes after induction), T2 (5 minutes after initiation of CPB), T3 (during the hypothermic phase of CPB), T4 (rewarming phase of CPB, at 34 °C), T5 (weaning from CPB), and T6 (upon admission to the intensive care unit).

During surgery, standardized interventions were performed if rSO_2 values decreased by more than 20% from the baseline to maintain cerebral oxygenation above this threshold [14]. These interventions included eliminating mechanical impediments to cerebral blood flow (such as repositioning of the head or bypass cannulas); improving cerebral oxygen delivery (by increasing FiO_2 , PaCO_2 , mean arterial pressure, cardiac output or pump flow, and hematocrit levels); and reducing cerebral oxygen consumption (by deepening anesthesia or lowering temperature). The overall aim was to restore physiological parameters that support adequate microcirculation [15].

2.6 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for MacOS, version 30.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test; skewness and kurtosis values within the range of ± 2 were considered sup-

portive of the normality assumption. Continuous variables that did not meet normality assumptions were presented as median and interquartile range [median (interquartile range [IQR])], while categorical variables were expressed as a number and percentage [n (%)]. Comparisons between the POCD and non-POCD groups were performed using the Mann–Whitney U test for continuous variables and the chi-square test or Fisher’s exact test, as appropriate, for categorical variables. Fisher’s exact test was specifically applied when one or more expected cell counts were less than 5, as the assumptions required for the chi-square test were not met in these cases.

Between-group comparisons of rSO₂ values at individual time points were conducted for exploratory purposes only. To evaluate time-dependent changes in intraoperative rSO₂ values and differences between groups, repeated measures analysis of variance (repeated-measures ANOVA) was applied. Repeated-measures ANOVA was used to evaluate within-subject time effects and group × time interactions. In these analyses, group (POCD vs non-POCD) served as the between-subject factor, and time (T0–T6) served as the within-subject factor. The assumption of sphericity was assessed using Mauchly’s test, and Greenhouse–Geisser correction was applied when the assumption was violated. Main effects of group, time, and group × time interaction were reported separately.

Repeated-measures ANOVA was also performed on percentage changes in rSO₂ relative to baseline (T1–T6) to assess time- and group-dependent differences. Associations between postoperative MMSE scores (POD4, POD7, and POD30), intraoperative rSO₂ percentage changes, and clinical outcomes (length of intensive care unit stay and hospital stay) were examined using Spearman’s rank correlation analysis. All statistical analyses were conducted using two-sided tests. $p < 0.05$ was considered to be statistically significant.

3. Results

Initially, 102 patients were enrolled in the study. Twenty-eight patients were excluded from the final analysis due to various reasons, including mortality, inability to perform postoperative MMSE assessments, or incomplete intraoperative NIRS data. The final analysis was conducted on 74 patients (Fig. 1). When evaluating the incidence of POCD after cardiac surgery, cognitive decline was identified in 32.4% of patients within the first postoperative week. This rate decreased to 20.2% at the 30-day follow-up.

Among the included patients, 33 (44.6%) were female, and 41 (55.4%) were male. The demographic and preoperative clinical characteristics of the POCD and non-POCD groups are presented in Table 1. Patients in the POCD group were significantly older than those in the non-POCD group (median [IQR]: 63 [58–68] vs. 59 [52–65] years, $p = 0.026$). There were no significant differences between the groups regarding sex distribution or EuroSCORE values ($p > 0.05$). Similarly, the prevalence of comorbidities, in-

cluding hypertension, diabetes mellitus, chronic pulmonary disease, hyperlipidemia, and peripheral arterial disease, did not differ significantly between the two groups ($p > 0.05$). In addition, the distribution of surgical procedure types was comparable between the POCD and non-POCD groups ($p = 0.908$).

A comparison of intraoperative and postoperative variables between the POCD and non-POCD groups is presented in Table 2. The durations of surgery, CPB, and ACC time were similar between the groups ($p > 0.05$). In the postoperative period, both ICU length of stay and total hospital stay were significantly longer in patients with POCD than in those without POCD (both $p < 0.001$). There were no significant differences between the groups regarding inotropic support, use of intra-aortic balloon pumps, pacemaker implantation, extubation time, requirement for continuous positive airway pressure or reintubation, arrhythmias, pneumonia, or surgical site infections ($p > 0.05$).

Intraoperative rSO₂ values, calculated as the average of bilateral frontal measurements, and their percentage changes relative to baseline are presented in Table 3. There were no significant differences between the POCD and non-POCD groups in T0 or T1 rSO₂ values ($p > 0.05$). In contrast, rSO₂ values were significantly lower in the POCD group at T2, T3, and T4 compared with the non-POCD group ($p < 0.05$), whereas no significant differences were observed between the groups at T5 or T6 ($p > 0.05$). The time-dependent trajectories of intraoperative rSO₂ values in both groups are illustrated in Fig. 2.

Repeated measures analysis of variance demonstrated a significant main effect of time ($p < 0.001$), indicating a marked change in rSO₂ values throughout the intraoperative period. The main effect of group was also significant ($p = 0.025$), suggesting an overall difference in rSO₂ levels between the POCD and non-POCD groups when all time points were considered together. In addition, a significant group × time interaction was observed ($p = 0.031$), indicating that the temporal pattern of rSO₂ changes differed between the two groups, as also visually demonstrated in Fig. 2.

When percentage changes in rSO₂ relative to baseline were evaluated, a significantly greater reduction was observed in the POCD group at T2, T3, and T4 compared with the non-POCD group. At T2, the median percentage change was –21.9% in the POCD group and –14.8% in the non-POCD group ($p = 0.005$). Similarly, greater desaturation was noted at T3 (–18.4% vs. –14.9%, $p = 0.003$) and T4 (–17.0% vs. –10.8%, $p < 0.001$). No significant between-group differences in percentage change were identified at T1, T5, or T6 ($p > 0.05$).

For percentage change values, repeated measures analysis revealed a significant main effect of time ($p < 0.001$), whereas the group × time interaction was not significant ($p = 0.115$). This finding suggests that, although the relative pattern of the change in rSO₂ over time was similar between the groups, absolute rSO₂ levels remained

Table 1. Patient baseline characteristics and preoperative data.

Variables	POCD (n = 24)	Non-POCD (n = 50)	p-value
Age (years), Median (IQR)	63 (58–68)	59 (52–65)	0.026
Female, n (%)	11 (45.8)	22 (44)	0.882
Male, n (%)	13 (54.2)	28 (56)	
EuroSCORE, Median (IQR)	4 (3–5)	4 (2–4)	0.065
Hypertension, n (%)	24 (100)	50 (100)	-
Diabetes mellitus, n (%)	14 (58.3)	28 (56)	0.850
Chronic pulmonary disease, n (%)	4 (16.7)	9 (18)	0.975
Hyperlipidemia, n (%)	11 (45.8)	23 (46)	0.989
Peripheral artery disease, n (%)	2 (8.3)	4 (8)	1.000
Categories of open-heart surgery			
Isolated CABG, n (%)	17 (70.9)	39 (78)	
CABG + Valve surgery, n (%)	2 (8.3)	4 (8)	0.908
Valve surgery only, n (%)	3 (12.5)	4 (8)	
Aortic surgery, n (%)	2 (8.3)	3 (6)	

Abbreviations: $p < 0.05$ considered statistically significant. n, Number of patients; IQR, Interquartile range; POCD, Postoperative cognitive dysfunction; CABG, Coronary Artery Bypass Grafting.

Table 2. Intraoperative and postoperative clinical outcomes.

Variables	POCD (n = 24)	Non-POCD (n = 50)	p-value
Operation time (min), Median (IQR)	262.5 (240–287.5)	262.5 (240–290)	0.949
CPB time (min), Median (IQR)	118 (91.5–152)	106.5 (84–125)	0.186
ACC time (min), Median (IQR)	86 (67.5–107.5)	71 (55–95)	0.146
Inotropic support			
No inotrope n (%)	-	2 (4)	
1 inotrope, n (%)	16 (66.7)	33 (66)	
2 inotrope, n (%)	5 (20.8)	12 (24)	0.950
3 inotrope, n (%)	2 (8.3)	3 (6)	
4 inotrope, n (%)	1 (4.2)	-	
IABP n (%)	1 (4.2)	1 (2)	0.546
Pacemaker use, n (%)	6 (25)	12 (24)	0.962
ICU stay (hours), Median (IQR)	74 (51.3–96)	50 (46–60)	<0.001
Hospital stay (days), Median (IQR)	9 (8–15.5)	7 (7–9)	<0.001
Extubation time (hours), Median (IQR)	8 (6–14)	7.8 (6–10)	0.542
CPAP requirement or reintubation n (%)	5 (20.8)	5 (10)	0.277
Arrhythmia, n (%)	18 (75)	38 (76)	0.925
Pneumonia n (%)	5 (20.8)	5 (10)	0.277
Surgical site infection, n (%)	2 (8.3)	4 (8)	1.000

Abbreviations: $p < 0.05$ considered statistically significant. n, Number of patients; IQR, Interquartile range; POCD, Postoperative cognitive dysfunction; CPB, Cardiopulmonary Bypass; ACC, Aortic Cross-Clamp; IABP, Intra-Aortic Balloon Pump; ICU, Intensive Care Unit; CPAP, Continuous Positive Airway Pressure.

consistently lower in the POCD group during specific intraoperative periods.

The correlations between intraoperative percentage changes in rSO_2 relative to baseline and postoperative cognitive performance are presented in Table 4. Significant positive correlations were observed between rSO_2 percentage changes at T2, T3, and T4 and MMSE scores on POD4 and POD30 ($p < 0.05$), indicating that greater intraoperative cerebral desaturation during these periods was associated with lower MMSE scores in the early and late postop-

erative phases. In contrast, no significant correlations were found between rSO_2 percentage changes and MMSE scores on POD7 ($p > 0.05$). No significant associations were observed for rSO_2 changes at T1, T5, or T6 with MMSE scores at any postoperative time point.

When factors potentially influencing MMSE scores were analyzed, the duration of ICU stay (hours) showed a significant negative correlation with MMSE scores on POD4, POD7, and POD30 ($r = -0.435$, $p < 0.001$; $r = -0.270$, $p = 0.020$; and $r = -0.413$, $p < 0.001$, respec-

Table 3. Intraoperative NIRS measurements and percentage changes relative to baseline.

NIRS Values, Median (IQR)	POCD (n = 24)	Non-POCD (n = 50)	<i>p</i> -value
T0 rSO ₂ , Median (IQR)	63.8 (62.3–68.5)	65.5 (61.5–69)	0.694
T1 rSO ₂ , Median (IQR)	69.8 (66–78.5)	71.5 (67–77)	0.673
T2 rSO ₂ , Median (IQR)	51.8 (47.3–55)	55.5 (50–59.5)	0.020
T3 rSO ₂ , Median (IQR)	52.8 (49.3–54.8)	56.5 (51.5–59)	0.002
T4 rSO ₂ , Median (IQR)	52.5 (49.3–56)	58 (54.5–63.5)	<0.001
T5 rSO ₂ , Median (IQR)	61.8 (56.5–63.5)	63.5 (57.5–68)	0.155
T6 rSO ₂ , Median (IQR)	61.8 (56.8–64.8)	62.8 (59.5–69.5)	0.212
NIRS percentage change values			
T0–T1 %, Median (IQR)	10.7 (6.5–15.3)	9.4 (5.8–15.7)	0.959
T0–T2 %, Median (IQR)	–21.9 (–25.1 to –15.3)	–14.8 (–19 to –9.6)	0.005
T0–T3 %, Median (IQR)	–18.4 (–25.5 to –15.7)	–14.9 (–18.8 to –8.7)	0.003
T0–T4 %, Median (IQR)	–17 (–21.5 to –15)	–10.8 (–15.7 to –3.6)	<0.001
T0–T5 %, Median (IQR)	–5.2 (–11.3–0)	–0.8 (–10.9–6.7)	0.179
T0–T6 %, Median (IQR)	–4.7 (–12.2–0.8)	–4.2 (–9.3–5.7)	0.239

Abbreviations: *p* < 0.05 considered statistically significant. n, Number of patients; IQR, Interquartile range; POCD, Postoperative cognitive dysfunction; rSO₂, Regional cerebral oxygen saturation; NIRS, Near-Infrared Spectroscopy; T0–T6, Measurement time points; T0, Preoperative period; T1, After induction; T2, Initiation of cardiopulmonary bypass (5th minute); T3, Hypothermic phase of CPB; T4, Rewarming phase of CPB; T5, Weaning from CPB; T6, Admission to the intensive care unit (ICU); CPB, Cardiopulmonary Bypass.

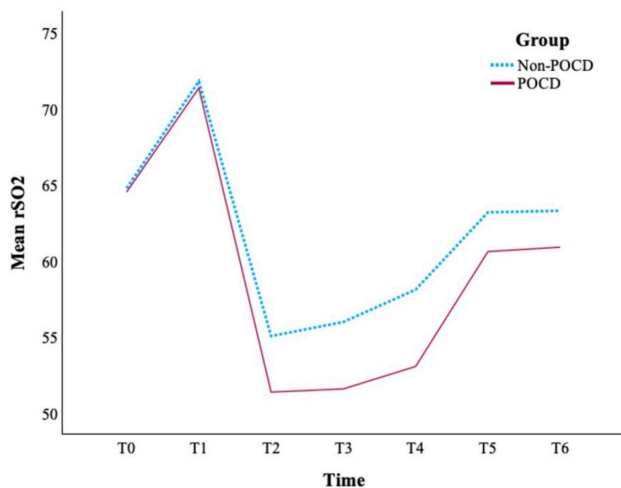


Fig. 2. Time-dependent changes in intraoperative rSO₂ values in POCD and non-POCD patients. T0, Preoperative baseline; T1, post-induction (15 min); T2, CPB initiation (5 min); T3, CPB hypothermic phase; T4, Rewarming phase of CPB; T5, Weaning from CPB; T6, ICU admission; rSO₂, Regional cerebral oxygen saturation; CPB, Cardiopulmonary Bypass; ICU, Intensive Care Unit.

tively). Similarly, the duration of hospital stay (days) was significantly and negatively correlated with MMSE scores at all postoperative time points (POD4: *r* = –0.428, *p* < 0.001; POD7: *r* = –0.319, *p* = 0.006; POD30: *r* = –0.489, *p* < 0.001). The association between hospital stay and POD30 MMSE scores is illustrated in Fig. 3 (Table 5). In contrast, no significant correlations were found between

Table 4. Intraoperative cerebral desaturation and MMSE correlation.

rSO ₂ (%)	POD4	POD7	POD30
T0–T1	<i>r</i> = –0.104 <i>p</i> = 0.377	<i>r</i> = 0.026 <i>p</i> = 0.827	<i>r</i> = –0.127 <i>p</i> = 0.279
T0–T2	<i>r</i> = 0.283 <i>p</i> = 0.014	<i>r</i> = 0.206 <i>p</i> = 0.078	<i>r</i> = 0.314 <i>p</i> = 0.006
T0–T3	<i>r</i> = 0.312 <i>p</i> = 0.007	<i>r</i> = 0.144 <i>p</i> = 0.221	<i>r</i> = 0.270 <i>p</i> = 0.020
T0–T4	<i>r</i> = 0.312 <i>p</i> = 0.007	<i>r</i> = 0.216 <i>p</i> = 0.065	<i>r</i> = 0.349 <i>p</i> = 0.002
T0–T5	<i>r</i> = 0.079 <i>p</i> = 0.506	<i>r</i> = –0.025 <i>p</i> = 0.832	<i>r</i> = 0.109 <i>p</i> = 0.356
T0–T6	<i>r</i> = 0.109 <i>p</i> = 0.353	<i>r</i> = 0.001 <i>p</i> = 0.995	<i>r</i> = 0.189 <i>p</i> = 0.107

Abbreviations: *p* < 0.05 considered statistically significant. *r*, Spearman rank correlation coefficient; POD, Postoperative day; MMSE, Mini-Mental State Examination; T0, Preoperative; T1, After induction; T2, Initiation of CPB (5th minute); T3, Hypothermic phase of CPB; T4, Rewarming phase of CPB; T5, Weaning from CPB; T6, ICU admission; CPB, Cardiopulmonary Bypass; ICU, Intensive Care Unit.

MMSE scores and the duration of surgery, CPB time, or ACC time (*p* > 0.05). These findings indicate a strong association between prolonged ICU and hospital stays and decreased early and late-postoperative cognitive performance (Table 5).

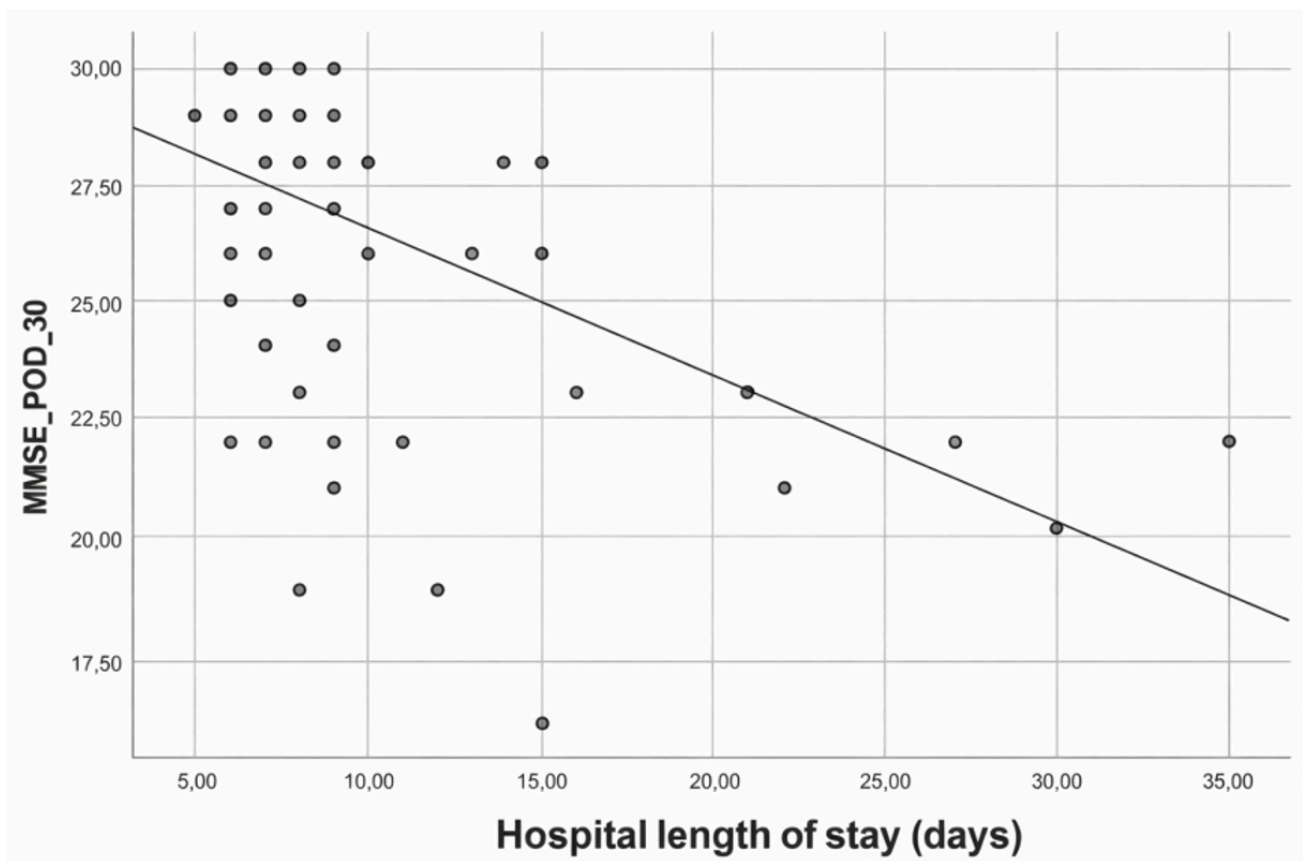


Fig. 3. Relationship between hospital length of stay and MMSE score on postoperative day 30. MMSE, Mini-Mental State Examination; POD, Postoperative day.

Table 5. Correlation between potential factors and MMSE scores.

Variables	POD4	POD7	POD30
	MMSE	MMSE	MMSE
Operation time (min)	$r = 0.040$ $p = 0.737$	$r = 0.034$ $p = 0.773$	$r = 0.110$ $p = 0.349$
CPB time (min)	$r = -0.096$ $p = 0.415$	$r = -0.086$ $p = 0.465$	$r = -0.117$ $p = 0.322$
ACC time (min)	$r = -0.114$ $p = 0.333$	$r = -0.135$ $p = 0.251$	$r = -0.166$ $p = 0.157$
ICU stay (hours)	$r = -0.435$ $p < 0.001$	$r = -0.270$ $p = 0.020$	$r = -0.413$ $p < 0.001$
Hospital stay (days)	$r = -0.428$ $p < 0.001$	$r = -0.319$ $p = 0.006$	$r = -0.489$ $p < 0.001$

Abbreviations: $p < 0.05$, considered statistically significant; r , Spearman rank correlation coefficient; POD, Postoperative day; MMSE, Mini-Mental State Examination; CPB, Cardiopulmonary Bypass; ACC, Aortic Cross-Clamp; ICU, Intensive Care Unit.

4. Discussion

In this prospective observational study, intraoperative cerebral oxygen desaturation during cardiopulmonary by-

pass was significantly associated with postoperative cognitive dysfunction, with greater intraoperative rSO_2 reductions observed in patients who developed cognitive impairment.

Despite significant advances in surgical safety measures and anesthesia management, POCD following cardiac surgery remains a major clinical challenge in terms of both prevention and management. POCD has been associated with adverse outcomes such as prolonged hospital stay, reduced quality of life, increased socioeconomic burden, and higher mortality rates [8]. With the progressive aging of the population, studies have reported that the incidence of POCD may reach up to 56% among individuals older than 55 years after surgery [16].

The variability in the reported incidence across studies may be attributed to heterogeneity in the neurocognitive assessment tools, timing of postoperative testing, the absence of a universally accepted definition of POCD, and differences in the cardiovascular risk profile and surgical techniques of the studied populations [17]. Early postoperative cognitive impairment is a significant predictor of subsequent POCD, and this association persists up to three months postoperatively [18–20]. Therefore, early identification of cognitive decline and implementation of appropriate follow-up strategies are crucial for reducing the long-term risk of dementia.

A total of 102 patients were initially screened, and 74 were included in the final analysis after applying exclusion criteria (Fig. 1). The incidence of POCD was 32.4% during the first postoperative week and decreased to 20.2% by postoperative day 30, reflecting an early decline followed by partial recovery over time. Baseline characteristics were comparable between the POCD and non-POCD groups regarding sex distribution, comorbidities, and types of surgical procedures; however, patients in the POCD group were significantly older than those without POCD (Table 1). Although EuroSCORE values tended to be higher in the POCD group, this difference did not reach statistical significance and remained at a borderline level. These findings suggest that advanced age represents a key patient-related factor associated with the development of POCD, whereas overall perioperative risk burden, as reflected by EuroSCORE, may contribute but does not independently discriminate between groups. Halacli *et al.* [21] also reported that increasing age and comorbidity burden adversely influence clinical outcomes in critically ill patients. The comparable distribution of surgical procedures between the two groups further minimizes procedure-related confounding, supporting the interpretation that the observed differences are primarily related to patient-level vulnerability rather than surgical factors. Future studies employing multivariable analytical models are warranted to better delineate the independent contribution of age and other perioperative risk indicators for the development of POCD.

Although the duration of CPB and ACC was longer in the POCD group than in the non-POCD group, these differences were not significant (Table 2). Therefore, no significant association between CPB and ACC durations and POCD was found in this cohort. Nevertheless, previous studies have suggested that prolonged CPB and ACC times may be associated with a tendency toward cognitive decline [22,23]. Thus, the observed numerical differences, although non-significant, should be interpreted with caution and considered hypothesis-generating rather than confirmatory. De Backer *et al.* [24] demonstrated that microcirculatory flow is markedly impaired during CPB, which may subsequently compromise postoperative organ function. Such microcirculatory disturbances, in conjunction with an intensified systemic inflammatory response, can lead to tissue hypoperfusion and oxygen deficit—mechanisms recognized as key contributors to the pathogenesis of POCD [25]. Related complications such as atrial fibrillation, acute kidney injury, and prolonged mechanical ventilation may represent clinical manifestations of these shared pathophysiological pathways. Similarly, systemic inflammatory mechanisms leading to multiorgan dysfunction have also been emphasized in critical care studies investigating severe illness [26].

In the present study, extubation time did not differ significantly between the POCD and non-POCD groups (Table 2). Postoperative complication rates were also compara-

ble between groups. However, both ICU length of stay and total hospital stay were significantly prolonged in patients who developed POCD (Table 2). These findings are consistent with the results of Zhuang *et al.* [27], who reported that prolonged ICU stay after CPB has been associated with an increased risk of postoperative cognitive decline. These findings suggest that POCD is more closely associated with a prolonged postoperative recovery process rather than parameters of intraoperative duration.

Studies in the field of cardiovascular surgery have demonstrated that non-pulsatile blood flow, inflammatory response, hemodilution, and hypothermia during CPB can markedly impair microcirculation, disrupting mitochondrial oxygen balance at the cellular level and contributing to the development of various complications, including POCD [28,29]. Findings from neuromonitoring research further support the contribution of cerebral hypoperfusion to the pathogenesis of POCD. Studies using NIRS have shown that intraoperative decreases in cerebral oxygen saturation are associated with postoperative cognitive changes, and that early episodes of cerebral desaturation may serve as valuable predictors for the development of POCD [10,11].

These findings are consistent with the results of the present study. Significant intraoperative changes in rSO_2 values were observed following the initiation of CPB (Table 3, Fig. 2). In the POCD group, rSO_2 levels were significantly lower than those in the non-POCD group during the intermediate intraoperative phases, specifically at T2, T3, and T4. In contrast, no significant between-group differences were observed at later time points (T5 and T6). Furthermore, analyses of percentage changes relative to preoperative baseline values revealed more pronounced cerebral desaturation in the POCD group during the same intermediate intraoperative phases. Although absolute rSO_2 levels differed between the groups, analyses of percentage changes suggested a similar temporal pattern over time, consistent with the absence of a significant group \times time interaction. These findings reinforce the association between intraoperative reductions in cerebral oxygenation—particularly during critical phases of CPB—and postoperative cognitive impairment.

Neuropsychological assessments performed in the early postoperative period may be influenced by multiple factors, including pain, residual effects of anesthetic agents, pharmacologic interventions, and sleep disturbances [30]. Therefore, early postoperative declines in cognitive performance cannot be entirely attributed to changes in cerebral oxygenation alone. In the present study, significant positive correlations were identified between intraoperative percentage changes in rSO_2 during the CPB (T2, T3, and T4) and MMSE scores assessed on POD4 and POD30 (Table 4). These findings suggest that more pronounced cerebral desaturation during these critical intraoperative periods is associated with lower cognitive performance in both the early and late postoperative phases.

In contrast, no significant correlations were observed between rSO₂ percentage changes and MMSE scores on POD7, indicating that the relationship between intraoperative cerebral oxygenation and cognitive performance may vary over time. Furthermore, no significant associations were identified between rSO₂ changes at T1, T5, or T6 and MMSE scores at any postoperative assessment. These results suggest that cerebral desaturation occurring during the intermediate phases of CPB (T2–T4) is more closely associated with early and late postoperative cognitive performance than desaturation observed at other intraoperative time points. Nevertheless, given the observational nature of this study, larger prospective investigations are warranted to define clinically meaningful desaturation thresholds and clarify the temporal sensitivity of different intraoperative periods in relation to postoperative cognitive trajectories.

Previous studies have demonstrated that alterations in rSO₂ values and impaired cerebral autoregulation—particularly during phases of increased cerebral metabolic demand such as rewarming—may be associated with postoperative cognitive decline [31]. In the present study, significant associations between intraoperative rSO₂ percentage changes and postoperative cognitive performance were observed during the initiation and hypothermic phases (T2–T3), particularly during the rewarming phase (T4) of CPB. These findings suggest that periods of increased vulnerability to cerebral desaturation during CPB may be relevant to subsequent cognitive outcomes.

Heterogeneity in desaturation thresholds, intraoperative intervention protocols, and POCD assessment methods has been identified as a major source of variability amongst studies. Zhang *et al.* [32] reported that the relationship between rSO₂ changes and POCD was particularly evident during the rewarming phase on postoperative day 7; however, their intervention strategy was limited to adjustments of mean arterial pressure and head positioning. Similarly, Uysal *et al.* [33] defined an intervention threshold of rSO₂ <60% for more than 60 consecutive seconds in both probes and reported higher memory scores at 6 months in the intervention group compared with controls. Although direct comparisons with these studies are limited by methodological differences, the existing literature underscores the importance of both the timing and the scope of intraoperative cerebral oxygenation management in shaping postoperative cognitive trajectories.

Future studies with larger sample sizes, standardized intervention thresholds, and comprehensive statistical models are warranted to clarify the specific impact of intraoperative rSO₂ fluctuations—particularly on late (30-day) cognitive outcomes. In addition, several studies have shown that prolonged ICU and hospital stays are associated with impaired cognitive function [27,30]. Consistent with these findings, our study demonstrated a significant negative correlation between both ICU and total hospital stay durations and MMSE scores at POD4 and POD30 (Table 5, Fig. 3).

These findings underscore the importance of implementing strategies such as early mobilization, maintenance of environmental orientation, and delirium prevention protocols, particularly in elderly patients at risk for cognitive impairment. Optimization of ICU and hospital length of stay durations, together with measures aimed at reducing postoperative complications and delirium, may represent an important component of multimodal approaches to support cognitive recovery within the multifactorial framework contributing to the development of POCD. Furthermore, Bendikaite and Vimantaite reported that cognitive impairment following cardiac surgery has not only early postoperative morbidity implications but also lasting effects on patients' quality of life [34]. Collectively, these observations highlight the necessity of adopting an integrated perioperative approach that simultaneously addresses hemodynamic stability and neurocognitive monitoring to mitigate postoperative cognitive dysfunction.

Limitations and Strengths

This study has several limitations. First, cognitive function was assessed only during the early postoperative period (within the first 30 days), and long-term neurocognitive outcomes were not evaluated. This limits the ability to determine whether POCD represents a transient or persistent condition. Second, although patients with clinically evident postoperative delirium were excluded based on routine clinical examination, delirium was not systematically assessed using standardized diagnostic tools, and other potential confounding factors that may influence MMSE scores in the postoperative period—such as pain level, sleep quality, and pharmacologic interventions—were not formally quantified. Therefore, the cognitive changes observed during this period cannot be exclusively attributed to surgical factors or cerebral oxygenation. Third, cognitive evaluation relied solely on the MMSE, and more comprehensive neuropsychological test batteries or alternative tools assessing attention and executive functions were not utilized. Finally, the single-center design and relatively small sample size may limit the generalizability of the findings. Nevertheless, the prospective design, multi-timepoint cognitive assessments, and the use of standardized intraoperative NIRS monitoring enhance the methodological strength of this study.

5. Conclusions

In this prospective observational study, intraoperative cerebral oxygen desaturation during cardiopulmonary bypass was found to be associated with postoperative cognitive dysfunction in patients undergoing cardiac surgery. More pronounced reductions in rSO₂, particularly during the rewarming (T4) phases of cardiopulmonary bypass and the subsequent initiation and periods of hypothermia (T2–T3), were related to poorer cognitive performance in both the early and late postoperative periods. In addition to intraoperative cerebral oxygenation patterns, patient- and

postoperative-related factors—most notably advanced age and prolonged intensive care unit and hospital stays—were consistently associated with lower postoperative MMSE scores.

These findings support the multifactorial nature of POCD and highlight intraoperative cerebral oxygenation as an important component within a broader perioperative risk profile rather than as an isolated determinant of cognitive outcome. Continuous intraoperative monitoring of cerebral oxygen saturation using near-infrared spectroscopy may contribute to the early identification of cerebral hypoperfusion and support timely corrective interventions, particularly in patients at increased risk of cognitive impairment following cardiac surgery.

Future large-scale, multicenter studies employing standardized intervention thresholds and comprehensive analytical models are warranted to further clarify the clinical relevance of intraoperative rSO₂ changes and better characterize their relationship with short- and long-term postoperative cognitive trajectories.

Availability of Data and Materials

The data generated and analysed during this study are presented in this article. Additional details or datasets are available from the corresponding author upon reasonable request.

Author Contributions

SBU conceived and designed the study, coordinated the data analysis, drafted the manuscript, and served as the corresponding author. BÖ contributed to data interpretation, manuscript writing, and critical revision of the manuscript. KÖ performed the statistical analyses, contributed to data visualization, and critically reviewed the manuscript for important intellectual content. MHU participated in data collection and patient follow-up and critically reviewed the manuscript. GG contributed to the literature review, clinical interpretation of the findings, and critical revision of the manuscript. DBG assisted in data verification, ethical documentation, and critical revision of the manuscript. MG contributed to the study design, supervised the overall project, and critically reviewed the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital (approval date: February 22, 2023; protocol no: 2011-KAEK-25 2023/02-15). Written informed consent was obtained from all participants prior to inclusion in the study.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used ChatGPT-5 (OpenAI) to assist in improving the clarity and fluency of the English language and to check grammar consistency. The authors subsequently reviewed, revised, and approved all contents of the manuscript, and take full responsibility for the integrity and accuracy of the published work.

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