Heart Surgery Forum 2024; 27(7): E718–E724
doi: 10.59958/hsf.7499
https://journal.hsforum.com/

Article

Investigation of the Effect of Cardiopulmonary Bypass on Optic Nerve Sheath Diameter

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Submitted: 29 March 2024 Revised: 9 May 2024 Accepted: 15 May 2024 Published: 7 July 2024

Abstract

Objective: We sough to evaluate the effects of cardiopulmonary bypass (CPB) on the intracranial area using ultrasound-guided optic nerve sheath diameter (ONSD), a noninvasive and easy to use technique. **Methods**: We prospectively studied 67 patients aged 18–80. Ultrasound (USG) measured the ONSD of the patients, and the threshold ONSD was accepted as 5.5 mm. Patients were divided into two groups according to ONSD during CPB. Group 1: ONSD less than 5.5 mm, and Group 2: ONSD at or greater than 5.5 mm. Demographic data, comorbidities, intraoperative and postoperative findings, and complications were recorded. **Results**: There was no difference between the groups regarding demographic data and comorbidities ($p > 0.05$). The amount of fresh frozen plasma and erythrocyte suspension transfusions were statistically significantly higher in Group 2 ($p < 0.05$). Bleeding between the groups, intravenous fluid administered, and urine output were higher in Group 2 but was not statistically significant. There was no statistical difference in the mean extubation time, intensive care and hospital stay, and postoperative complications between the groups ($p > 0.05$). There was no mortality in Group 1, but two patients in Group 2 died. A statistically significant increase on ONSD was observed in Group 2 compared to Group 1 ($p < 0.001$). **Conclusion**: We observed that the increase in ONSD was greater in open heart surgeries that required increased blood and blood product transfusion. However, prospective studies are needed to investigate its clinical effects.

Keywords

optic nerve; cardiopulmonary bypass; cardiac surgery

Introduction

Cardiopulmonary bypass (CPB) in cardiac surgery is associated with a risk of developing neurological complications in the early and late postoperative period. One of the two essential components of the heart-lung machine, is the oxygenator, which acts as the lung, and the pump, which acts as the heart. The perfusion system during CPB can provide full or partial circulatory and respiratory support. The non-pulsatile flow during CPB is not physiologic organs. Furthermore, changes in vascular resistance during perfusion also affects the perfusion of tissues [1], resulting in and central nervous system injury, due to low perfusion and ischemia. In addition flow, arterial and venous pressures, pre- and post-capillary resistances, and viscosity during CPB affect fluid extravasation. The relative importance of each factor in the development of tissue edema is unknown.

Optic nerve sheath diameter (ONSD) measured by ultrasonography (USG) is a non-invasive, fast, and easily applicable method for determinging changes in intracranial pressure. Noncardiac surgery studies have found high sensitivity and specificity in predicting intracranial pressure (ICP) >20 mmHg if ONSD is >5.5 mm [2,3]. Studies have found that monitoring high intracranial pressure (ICP) levels with USG and ONSD has an important predictive value in open heart surgery [4,5].

In this study, we sought to evaluate the effects of hemodilution during CPB with USG-guided ONSD.

Material and Methods

Following the approval of protocol 2011-KAEK-25 2018/11-07 from the University Hospital of High Specialization and Education, Bursa Ethics Committee, and written consent of the patients. Exclusion criteria included the presence of an intracranial mass, orbital or orbital tumor, patients who arrested after surgery or required re-exploration patients with suboptimal USG image, and patients who underwent ultrafiltration. Initially100 cardiac surgery patients between the ages 18–80 on CPB were included. 33 patients were excluded (Fig. 1). Demographic data of the patients, age, gender, weight, American Society of Anesthesiologists (ASA), other diseases, and medical treatments were recorded.

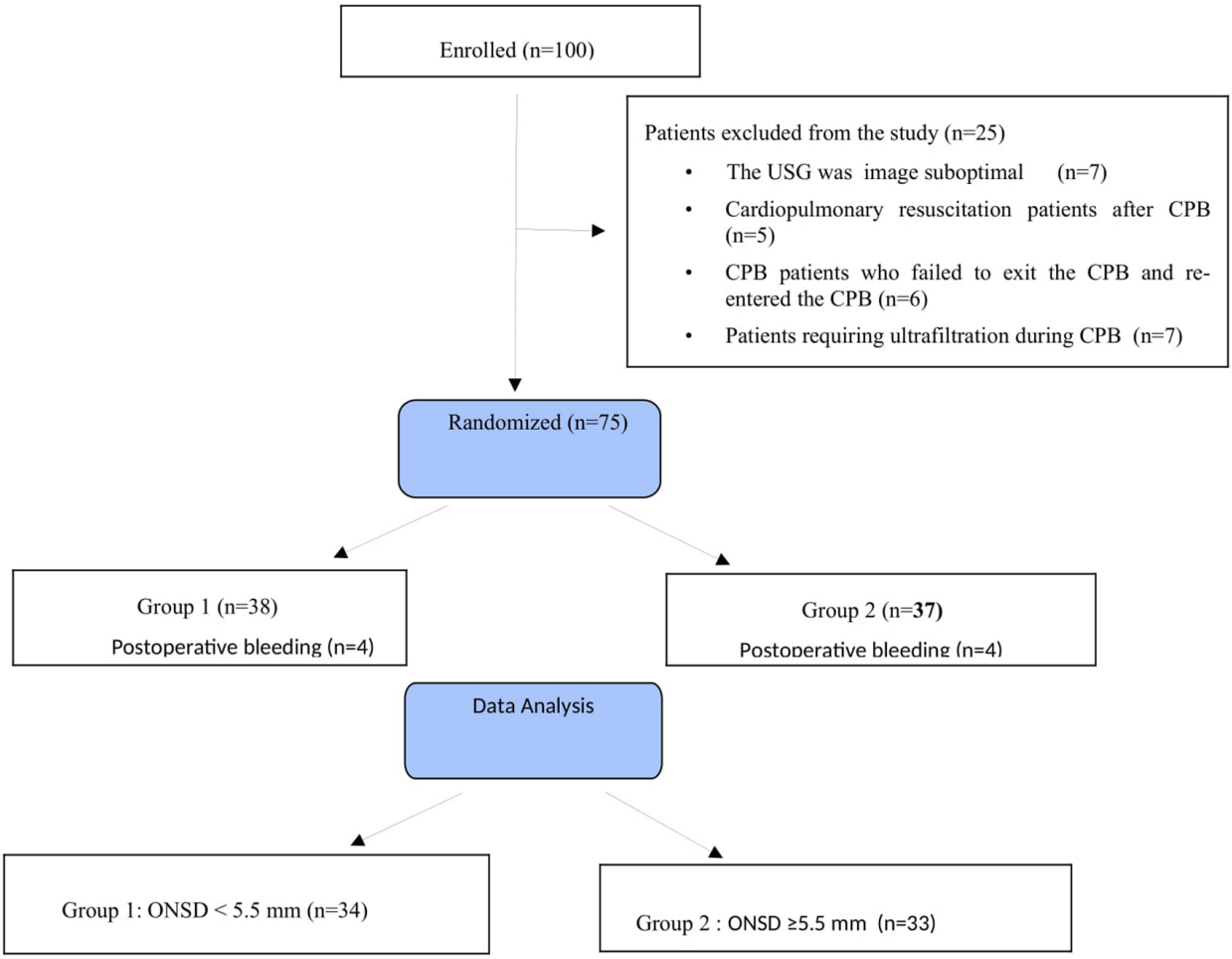

Fig. 1. Flow chart of the procedure. USG: Ultrasonography; CPB: Cardiopulmonary bypass; ONSD: Optic nerve sheath diameter.

Anesthesia Management

Patients were premedicated with IV midazolam intravenous (Zolamid ®, Defarma, Tekirdag, Turkey) (0.05–0.1 mg/kg) in the operation room, and underwent systemic arterial pressure monitoring by radial artery cannulation. Anesthesia induction consisted of fentanyl (Talinat ®, Vem, Istanbul, Turkey) (1–2 µg/kg, iv) and propofol 1% Fresenius (Pofol ®, Aroma, Istanbul, Turkey) (1–2 mg/kg), and rocuronium bromide (Curon ®, Mustafa Nevzat, Istanbul, Turkey) (0.6 mg/kg, iv). Fresh gas entry was 2 lt/min, tidal volume was 6–8 mL/kg, FiO_2 was 0.5, frequency was 10–12/min and positive end-expiratory pressure (PEEP) was 5. Anesthesia was maintained with 0.1–0.3 mg/kg rocuronium, 0.02 mg/kg midazolam and 0.5 mcg/kg fentanyl under Bispectral Index (BIS) monitoring. Sevoflurane (Sevorane, Abbott, Turkey) was administered to keep the minimal alveolar concentration (MAC) between 0.8 and 1.2. An internal jugular central venous catheter and a urinary catheter was inserted, and urine output was monitored. Temperature monitoring was also provided. 6–8 mL/kg of intravenous fluid was given before CPB anticoagulation was established with anti-fractionated heparin (Koparin Vial, Kocak Farma, Turkey) at a dose of 300 Units/kg and activated clotting time (ACT) was measured. Arterial blood gas was also measured concurrently with the ACT. CPB was initiated when the ACT exceeded 450 seconds.

CPB Management

Cardiac arrest was achieved with a cold cardioplegic solution. The temperature was maintained at 31–32 °C during CPB. The perfusion pressure (PB) was adjusted to maintain a mean arterial pressure (MAP) of 60 to 70 mm Hg. Myocardial viability was maintained with antegrade cold hyperkalemic crystalloid cardioplegia according to a standard protocol. Arterial blood gas was analyzed every 30 minutes. Following CPB, anticoagulation was neutralized with protamine sulfate at a dose of 350 Units/kg. Arterial blood gas was also analyzed simultaneously with ACT after protamine administraton. Hemofiltration and autologous red blood cell transfusion was utilized to maintain a hematocrit (Hct) level above 20%. Hematocrit change in the pump and arterial blood gas analyzes during hemodlation give us an idea about the need for transfusion. The amount of bleeding will also be calculated from the volume accumulated in the aspirators.

Based on retrospective data, an ONSD was below 5.5 mm at any time was classified as Group 1; if it was 5.5 mm or above it was classified as Group 2.

Measurements

Hemodynamic parameters, SpO_2, urine output; aortic cross-clamp (CC) and CPB duration, perfusion pressures (PP) and hypothermia, Hct, blood transfusion were recorded. Measurement times consisted of ONSD before anesthesia induction (T0), after induction (T1), during CPB and hypothermia (T2), and after CPB (T3). Extubating time, postoperative complications and mortality (within 10 days postoperatively) were also recorded.

ONSD Measurement

A linear 5–10 MHz ultrasound probe (GE HealthCare Technologies, Chicago, Illinois, USA) was placed on the upper eyelid over the gel. The orbital optic nerve was in 2 dimensional (2D) mode with no excessive pressure. The entrance to the globe was displayed. After finding the optimal contrast between the retrobulbar echogenic adipose tissue and the vertical hypoechogenic band, the ONSD was measured 3 mm behind the optic disc by the same blinded anesthesiologist (Fig. 2). Patients whose optic disc could not be seen clearly during USG measurement or whose accuracy was questionable and whose contrast discrimination was not clear were excluded from the study.

Statistical Analysis

Statistical analyses were performed using the IBM SPSS 24 program (IBM SPSS statistics, Chicago, IL, USA). The demographic and clinical data were expressed as the mean ± standard deviations for continuous variables and numbers (percentages) for categorical variables. The Kolmogorov-Smirnov tests were used to analyze the normal distribution of measurements. The chi-square test was used in group comparisons if the frequency was compared for categorical variables. The independent sample *t*-test was applied if mean values were compared for continuous variables. Statistical significance in the analyses was accepted as $p < 0.05$. The power of our study was measured as effect size 0.7, $\alpha = 0.05$, Power (β) = 80% with 67 patients.

Results

The study was conducted on a total of 67 patients, 18 females and 49 males. When both groups were compared in terms of demographic data and preoperative cardiac risk factors, no statistical difference was found ($p > 0.05$) (Table 1). The number of patients who underwent emergency surgery was 2 patients (5.9%) in group 2, but none in group 1 (Table 1).

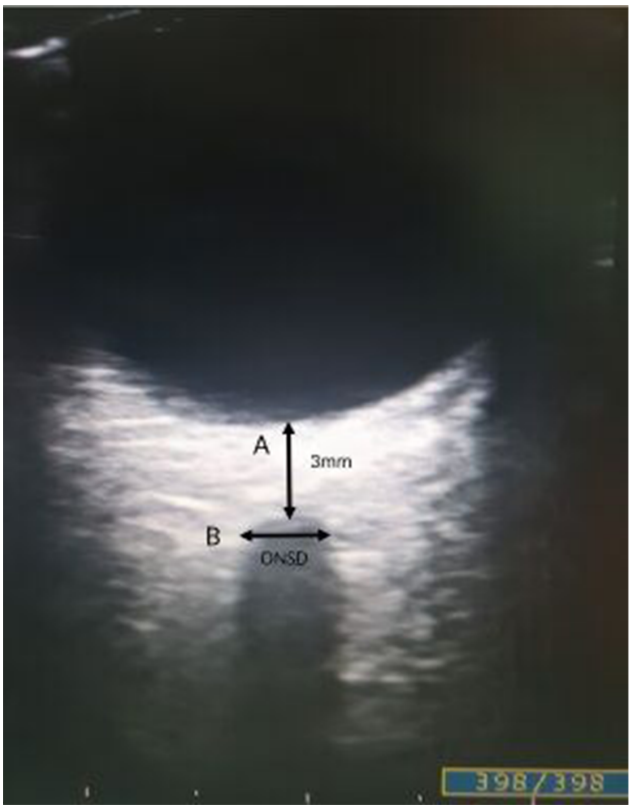

Fig. 2. Optic nerve sheath diameter measurement (ONSD). (A) Optical disc. (B) Optic nerve sheath diameter.

Table 1. Preoperative cardiac risk factors and demographic data comparison of the study groups.

	Group 1	Group 2	*p
Age (years) (mean ± SD)	62.30 ± 10.40	59.70 ± 9.70	0.30
Gender (n, %)			
Male	24, 70.6%	25, 75.8%	0.63
Female	10, 29.4%	8, 24.2%	
BMI (kg/m^2) (mean ± SD)	29.90 ± 4.30	29.50 ± 5.30	0.71
EF % (mean ± SD)	49.44 ± 9.21	50.88 ± 8.97	0.52
ASA (n, %)			
ASA III	27, 79.4%	22, 66.7%	0.23
ASA IV	7, 20.6%	11, 33.3%	
Euroscore (mean ± SD)	4.50 ± 2.43	4.39 ± 2.79	0.86
Urgent (n , %)	2, 5.9%	0	-
Hypertension (n, %)	25, 73.5%	30, 90.9%	0.16
Diabetes mellitus (n,%)	13, 38.2%	14, 42.4%	0.65
Cerebrovascular disease (n, %)	3, 8.8%	4, 12.1%	0.51
Peripheral arterial disease (n, %)	6, 17.6%	4, 12.1%	0.27
Hyperlipidemia (n, %)	8, 23.5%	5, 15.1%	0.19

SD, Standard deviation; BMI, Body mass index; EF, Ejection fraction; ASA, American Society of Anesthesiologists.

The groups were statistically similar in terms of heart rate, mean arterial pressure, and perfusion pressure (Table 2).

The anesthesia duration, blood transfusion volume and Hct changes between preoperative and postoperative

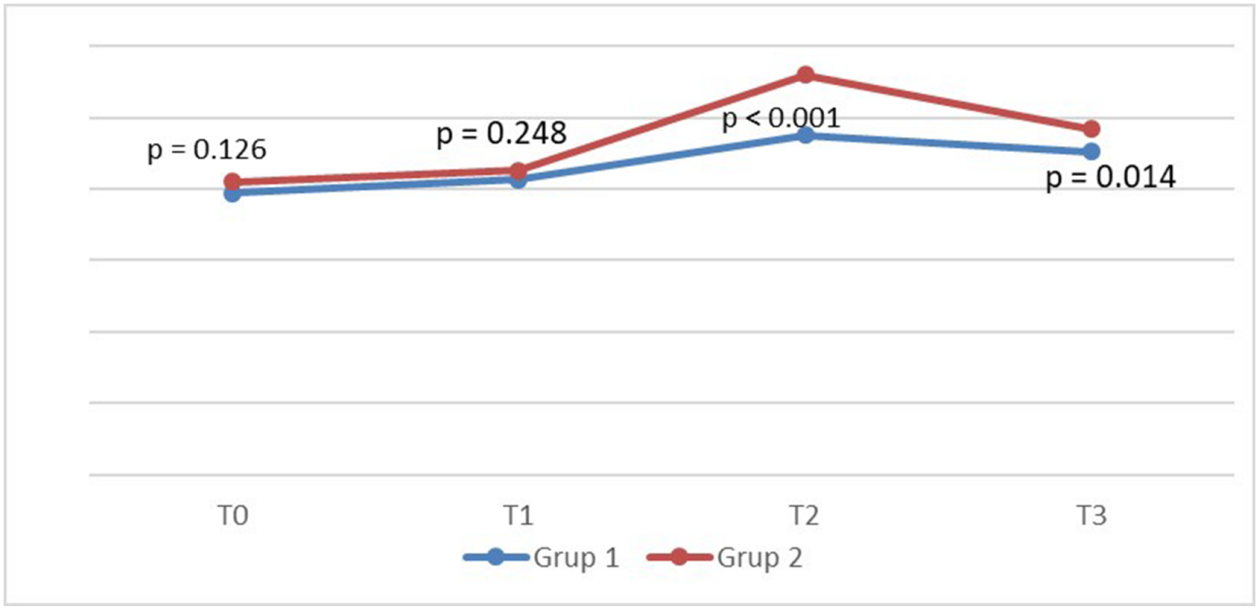

Chart 1. Comparison of ONSD values between the groups at measurement times. T0: Before anesthesia induction, T1: After induction, T2: During cardiopulmonary bypass and hypothermia, T3: After cardiopulmonary bypass.

Table 2. Comparison of hemodynamic data of group.

	Group 1	Group 2	*p
HR (T0) (beat/minute)	87.46 ± 11.36	82.11 ± 0.22	0.152
HR (T1) (beat/minute)	80.13 ± 11.74	75.46 ± 13.09	0.062
HR (T3) (beat/minute)	111.94 ± 21.30	110.18 ± 20.61	0.732
MAP (T1) (mm/Hg)	97.35 ± 14.84	95.15 ± 15.63	0.556
MAP (T2) (mm/Hg)	75.94 ± 9.93	76.18 ± 19.96	0.950
MAP (T3) (mm/Hg)	66.00 ± 7.49	65.61 ± 8.67	0.848
PP (T2) (mm/Hg)	134.41 ± 11.92	143.03 ± 23.81	0.064

HR, Heart rate; MAP, Mean arterial pressure; PP, Perfusion pressure. T0: Anesthesia induction, T1: After induction, T2: During CPB and hypothermia, T3: After CPB.

periods were statistically significantly higher in Group 2 ($p = 0.05$, $p = 0.006$, $p = 0.004$ and $p = 0.030$, respectively) (Table 3). The duration of surgery, CPB and CC; number of patients need for inotropic infusion or an intra-aortic balloon pump, hypothermia level, extubating time, intensive care and hospital stay, and postoperative complications was similar between the groups. Bleeding volume, intravenous fluid and urine output was higher but not statistically significant in Group 2 (Table 3).

Mortality was not seen in Group 1 but occurred in two patients in Group 2.

A statistically significant increase was observed in ONSD in Group 2 at times T2 and T3 ($p < 0.001$) (Chart 1).

Discussion

Cardiac surgery with CPB, blood transfusions and increased Hct are associated with increased ONSD. Extubation times, intensive care and hospital stays, and mortality were similar between the groups.

Hemodilution and inflammation are important concerns during CPB. Hemodilution disrupts oxygen transport throughout the tissues, and triggers an extensive inflammatory reaction which disrupts tissue perfusion, and affects mortality and morbidity. A study in rats on the changes in hemodilution in the optic nerve found that intraoperative ischemic injury results in optic neuropathy and optic nerve damage [6]. Studies have reported that adverse neurological outcomes following coronary artery bypass graft (CABG) surgery may be related to embolic effects, hypoxic-ischemic events, changes in autoregulation, the blood-brain barrier, and intracranial pressure (ICP) changes [7,8]. The brain is one of the most affected organs during CPB, since the the brain receives up to 15% of the cardiac output. The inability to perform invasive intracranial imaging has led to non-invasive imaging. Ultrasonographic evaluation of ONSD has been a promising and reliable non-invasive technique for ICP [9].

Taskin O *et al*. [5] found that ONSD measurements during extracorporeal circulation in cardiac surgery is an easy, inexpensive and low-complication method that can be performed at the bedside during surgery to monitor ICP changes. In another study, negative neurological outcomes were evaluated by measuring ONSD during open heart surgery and found that ONSD diameter measurements were useful in predicting neurological outcomes [4].

Subarachnoid, pia mater and arachnoid space cover the brain, which lies between the maters. It is filled with cerebrospinal fluid and is continuous with the perineural space of the optic nerve. Pressure changes affecting the

Table 3. Comparing the perioperative clinical characteristics, replacements, and mortality between the study groups.

	Group 1	Group 2	*p
Operation time (mean ± SD) (minute)	202.41 ± 56.10	224.21 ± 53.69	0.109
CPB duration (mean ± SD) (minute)	106.21 ± 34.99	112.30 ± 31.39	0.456
Aortic cross clamp time (mean ± SD) (minute)	74.03 ± 30.82	80.67 ± 24.94	0.337
Total amount of fluid given (mean ± SD) (mL)	1375.75 ± 206.20	1429.41 ± 191.53	
Urine amount (mean ± SD) (mL)	1075.88 ± 507.28	1147.57 ± 541.70	0.450
Bleeding amount (mean ± SD) (mL)	546.00 ± 85.34	584.00 ± 116.01	0.134
Patient with inotropic infusion therapy n (%)	19 (55.9)	21 (63.6)	0.518
IABP n (%)	2 (4)	2 (4)	
Degree of hypothermia (mean ± SD) (°C)	30.47 ± 2.02	30.82 ± 1.76	0.456
FFP infusion (mean ± SD) (Units)	2.03 ± 1.70	2.65 ± 1.23	0.006*
Erythrocyte suspension infusion (mean ± SD) (Units)	1.00 ± 1.37	2.15 ± 1.71	0.004*
Changing in preop and postop Hct (mean ± SD) (%)	26.16 ± 9.57	31.03 ± 8.37	0.030*
Extubating time (mean ± SD) (hours)	7.91 ± 2.86	7.97 ± 2.19	0.926
Intensive care unit hospitalization time (mean ± SD) (hours)	68.53 ± 38.58	63.85 ± 42.22	0.637
Postoperative complications n (%)	3 (6)	3 (6)	-
Mortality n (%)	-	2 (4)	

*$p < 0.05$ statistically significant. CPB, Cardiopulmonary bypass; IABP, Intraaortic balloon pump; FFP, Fresh frozen plasma; Preop, Preoperative; Postop, Postoperative; Hct, Hematocrit.

intracranial area extend to the ONSD. The increase in intracranial pressure is transmitted to the ONSD and expands its diameter [3]. A study has shown that ONSD was 5.4 mm in patients with increased ICP symptoms [2]. For the groups in our study, ONSD was defined as 5.5 mm.

In a cardiac surgery study, patients with optic neuropathy experienced a sudden or severe perioperative decrease in haemoglobin (Hgb) [7]. Decreased postoperative Hgb due to greater hemodilution, and the added prime solutions increase the risk of coagulopathy with CPB in cardiac surgeries [10]. Studies have shown increased retinal and cerebral ischemia in CPB [11,12]. It has been demonstrated that hypotension, arrhythmias, hypercoagulopathy, and hypothermia during surgery and CPB may decrease blood flow and increase ischemia in the optic area. Intraoperative risk factors for increased ICP include hypotension, anaemia/hemodilution, head-down positioning, lengthy surgery and vasopressors. Optic neuropathy was observed in a study on animals with hemodilution and head-down position [6]. Hemodilution is one of the inevitable requirements of CPB. Preoperatively, the Hct after the onset of CPB is estimated, considering the patient's preoperative Hct, the patient's circulating blood volume before surgery, and the volume of the priming solution for CPB. The filling volume is the fluid added to prime the cylinder pump, oxygenator, filters and tubing before connecting the venous and aortic cannulas. This volume will mix with the patient's blood at the start of CPB. However in some patients, the initial Hct measured after the onset of CPB may be unexpectedly lower than the acceptable predetermined value [1]. In this case, homologous blood can be added to the pump to improve oxygen delivery and prevent postoperative complications [13]. Excess hemodilution, and a Hct below 22%, results in increased neurocognitive impairment, stroke, acute renal failure, and mortality [14]. Considering the adverse effects of homologous blood transfusion, avoiding excessive hemodilution and transfusion is essential to reduce postoperative complications. It is impossible to estimate the actual circulating blood volume [15]. The volume of hydration until CPB will make it difficult to predict the expected Hct during CPB. Although there was no significant difference in the initial Hct or CPB preparation volume in one study, in patients who received >1600 mL of fluid before CPB, there was a decrease in mean low CPB Hct, an increased CPB Hct, and an increased transfusion of homologous red blood cells during CPB [16]. In our study, although the fluid volumes between the groups were similar, the change in Hct was different, suggesting that ONSD changes were associated with red blood cell transfusion. Minimally invasive surgical techniques, less fluid and blood product replacement during anesthesia, and higher blood pressure levels are recommended to preserve the optic field [17,18]. Increased ICP was observed in a study in head-injured dogs that had hemodilution with low Hct (27%) using equal amounts of crystalloid and colloid solutions [19]. In our study, an increase in ONSD was observed in Group 2, with a high Hct rate, increased blood transfusion, and hemodilution similar to reports in the literature. ONSD was higher in Group 2, especially during and after CPB. This may be related to increased hemodilution and an increased need for blood products.

In another study, prolonged CPB duration, lower Hct, increased 24-hour postoperative weight gain, and vasoactive drugs were associated with optical changes [20]. In our study, CPB duration and inotropic use were similar between the groups. Hct did not fall below 22%. MAP and PP during and after the CPB; pre-pump and post-pump heart rate (HR) and inotropic agents were similar between groups.

Limitations

The limitations of our study are the lack of pre- and postoperative optical field evaluation, the small number of cases, the lack of evaluation of postoperative clinical events, differences in surgical techniques, and the lack of simultaneous near-infrared spectroscopy (NIRS) monitoring. We did not examine inflammatory markers in this study.

Conclusion

The findings of increased ONSD in patients with greater requirements for blood and plasma transfusion during CPB could have significant implications for monitoring and managing patients at risk for increased intracranial pressure. This can lead to better patient outcomes through more tailored perioperative care.

Availability of Data and Materials

The supporting data and materials for the findings of this study can be obtained from the corresponding author upon request, subject to reasonable conditions.

Author Contributions

UK and BO analyzed data; UK, BO and TO conceived and supervised the study, designed this study and checked all the data; AO, ANB, and GE searched the databases; UK and ME conducted the meta-analysis; UK and TO analyzed the data and drafted the manuscript; AO and ME contributed to reviewing. All authors reviewed the results and approved the final version of the manuscript. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

After the approval of the decision numbered 2011-KAEK-25 2018/11-07 from the University Hospital of High Specialization and Education, Bursa Ethics Committee, written consent was obtained from all of the patients. The study was conducted in accordance with the Declaration of Helsinki and followed the ethical standards of Turkey. Importance was given to patient privacy and autonomy. Patient information was kept confidential.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflicts of interest concerning the authorship and publication of this article. The authors have no commercial associations or sources of support that might pose a conflict of interest. The authors certify that they have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript (e.g., employment, consultancies, stock ownership, and honoraria).

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