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The effects of total intravenous and inhalation anesthesia maintenance on tissue oxygenation in coronary artery bypass graft surgery

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Abstract. – OBJECTIVE: The aim of this study is to evaluate the effect of total intravenous anesthesia (TIVA) and inhalational anesthesia techniques on tissue oxygenation in cardiac surgery. We compared the effects of midazolam-based TIVA and sevoflurane-based (SEVO) inhalation anesthesia maintenance on intraoperative central and regional tissue oxygenation parameters.

PATIENTS AND METHODS: A total of 104 adult patients who were scheduled for elective isolated coronary bypass surgery were included in the study. All patients were divided into two groups: the TIVA group consisted of total intravenous anesthesia maintenance patients (n=52) and the SEVO group consisted of patients with inhalation anesthesia with sevoflurane maintenance (n=52). Tissue oxygenation values were observed with left-right cerebral and somatic left forearm Near-Infrared Spectroscopy (NIRS) sensors. The hemodynamic parameters, NIRS StO_2, central ($ScvO_2$) and peripheral venous oxygen saturations of the patients were recorded at six intraoperative time points.

RESULTS: The effects of midazolam-based TIVA and sevoflurane-based inhalation anesthesia maintenance on intraoperative central and peripheral tissue oxygenation parameters were compared and it was found that in the left forearm NIRS StO_2 and $ScvO_2$ values were higher in the SEVO group than the TIVA group. Although not significantly different, forearm regional venous oxygen saturation was also higher in the SEVO group.

CONCLUSIONS: The effects of anesthetic drugs on regional tissue oxygenation can become important in critical patients and challenging surgeries. Sevoflurane-based anesthesia provides better tissue oxygenation than TIVA in patients undergoing coronary bypass surgery.

Key Words:
Cardiac surgery, Tissue oxygenation, Total intravenous anesthesia, Inhalational anesthesia.

Introduction

A pressing issue in anesthesiology involves developing an understanding of the non-anesthetic effects of the medications typically used in intravenous and inhalation anesthesia methods. Few studies[1] describe the effects of both intravenous and inhalational anesthetics on regional tissue perfusion under stable anesthetic conditions. The specific issue is whether inhalational anesthetics compromise regional tissue perfusion even if systemic parameters are within normal ranges[1]. The question of what causes these effects to differ under pathophysiological conditions, such as cardiac surgery, is still under debate.

Maintaining tissue perfusion and oxygenation is the cornerstone of therapy for patients with cardiac disease. An imbalance in oxygen delivery and tissue oxygen consumption leads to anaerobic metabolism, cellular injury, and organ dysfunction, and is associated with poor outcomes. Consequently, monitoring tissue oxygen delivery and consumption status is of paramount importance in cardiac surgery patients. Routinely used monitors in intraoperative settings such as pulse oximetry, blood pressures, hemoglobin saturation levels, lactate, acid-base status, and central venous oxygen saturation levels all reflect tissue metabolism. Near-infrared spectroscopy (NIRS) is a non-invasive optical technique that can be used to continuously monitor tissue oxygen delivery and oxygen consumption status. Cerebral autoregulation can blunt the effect of impaired systemic oxygen delivery. Thus, cerebral NIRS may be a good predictor of neurological outcomes, but skeletal muscle NIRS serves as a follow-up indicator of many other postoperative complications due to impaired perfusion and ox-

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ygenation. Therefore, both cerebral and somatic monitoring may contribute to a more complete evaluation of hemodynamic competence[2]. Obtaining the cerebral and somatic oxygenation levels is an important component of clinical management during cardiopulmonary bypass (CPB) and cardiac surgery as a whole.

The aim of this study was to evaluate the effect of total intravenous anesthesia (TIVA) and inhalational anesthesia techniques on tissue oxygenation in cardiac surgery. To this end, the effects of midazolam-based TIVA and sevoflurane-based inhalation anesthesia maintenance on intraoperative central and somatic tissue oxygenation parameters were compared in patients undergoing cardiac surgery.

Patients and Methods

Study Population and Selection Criteria

The study protocol was approved by the institutional Ethics Committee (No: E-17-1692, Date: 03.01.2018) and written informed consent was obtained from each subject. The study was conducted in accordance with the principles of the Declaration of Helsinki. Exclusion criteria were as follows: a history of emergency surgeries, reoperations, ejection fraction under 40%, coronary surgeries in conjunction with other procedures, cerebrovascular accident, neurological disorder, hematologic disorder, or alcohol use, as well as the patient's age being under 18 years.

All patients were grouped in two according to anesthesia management: the TIVA group consisted of subjects administered total intravenous anesthesia maintenance (n=52); the SEVO group consisted of patients given inhalation anesthesia with sevoflurane maintenance (n=52). Demographic and clinical data, intraoperative data, postoperative complications, mortality, extubation time, intensive care unit (ICU) stay, and time to discharge were recorded.

Anesthetic Management

All patients were administered 0.15 $mg.kg^{-1}$ oral diazepam the night before surgery and 0.1 $mg.kg^{-1}$ morphine 30 minutes before surgery. The patients were taken to the operating room, and two peripheral veins and the left radial artery were cannulated. Pulse oximetry and 5 channel electrocardiography were performed, and invasive artery pressure was monitored. A bispectral index (BIS™, Covidien, MN, ABD) sensor was placed on the forehead. After preoxygenation, anesthesia induction with 10 $\mu g.kg^{-1}$ fentanyl and 0.15 $mg.kg^{-1}$ midazolam was performed. Once the BIS was stable between 40-50, 0.8 $mg.kg^{-1}$ of rocuronium was used to facilitate tracheal intubation. The lung was ventilated with 7-8 $ml.kg^{-1}$ tidal volume adjusted for ideal body weight with a mixture of O_2/air (FiO_2 0.5) and 5 $cm.H_2O$ PEEP. The respiratory rate was set to keep an end-tidal CO_2 pressure between 35-45 mmHg. Arterial oxygen pressure was optimized at 100-200 mmHg. During the maintenance of the anesthesia of the TIVA group, 3 $\mu g.kg^{-1}$ fentanyl, 0.01-0.05 $mg.kg^{-1}$ midazolam, and 0.2 $mg.kg^{-1}$ rocuronium bromide were applied throughout the operation to keep BIS between 40 and 60, approximately once every 45 minutes. During the anesthesia maintenance of the SEVO group, 2-3% sevoflurane (1-2 MAC), 3 $\mu g.kg^{-1}$ fentanyl, and 0.2 $mg.kg^{-1}$ rocuronium bromide were applied throughout the operation to keep BIS between 40-60. In the course of CPB, sevoflurane vaporizer designed for the pump was used. In the course of CPB, a sevoflurane vaporizer was designed, and by connecting the CPB oxygenator outlet to the central waste gas scavenging system in the operating room, pollution of the OR air is prevented, and personnel safety is ensured. End-tidal volatile anesthetic concentration (ETAC) and minimum alveolar concentration (MAC) values obtained from the oxygenator outlet are added to the EEG-based BIS monitor. It has been observed that BIS values of 40-60 can be achieved with a MAC value of 0.5 (ETAC 0.6-1.2) during CPB, which is probably associated with hypothermia. Oropharyngeal temperature was monitored. For blood gas management during CPB, the alpha-stat strategy was used. Hemoglobin concentrations were kept above 7.5 $g.dl^{-1}$ during the operation and above 8.5 $g.dl^{-1}$ after the operation. Administration of anesthetics was discontinued upon completion of the surgical procedure. Paracetamol and tramadol were used in analgesia management. Extubation was performed according to local ICU protocols.

Surgical Technique

After the left internal mammary artery was harvested with the heparinization, venous and aortic cannulas were inserted. CPB was initiated using a roller-pump, open reservoir, and Nipro® oxygenator with a target flow of 2.2-2.4 $L.min^{-1}$ per m^2 at 36°C (The Affinity NT Integrated Trillium CVR/Membrane Oxygenator, Medtronic, Minneapolis, MN, USA).

Prime volume composition was composed of ringer lactate solution and other additives. CPB was performed in moderate hypothermia (30-32°C). After cardiac arrest was performed with anterograde crystalloid cardioplegia (Plegisol®), it was maintained using 1:4 ratio mixed blood by retrograde cardioplegia at 20-min intervals. After distal anastomosis, cross-clamp was removed by applying hot blood cardioplegia, and proximal anastomosis was, then, performed by side clamping. After decannulation, the heparin effect was reversed by protamine, the cardiopulmonary bypass was terminated, and the sternum was closed after bleeding control.

Tissue Oxygenation Monitoring

In addition to standard monitoring, the forehead and forearm skin were cleaned and NIRS (INVOS Somanetics, 5100, Troy, MI, USA) sensors were placed into the bilateral frontal area 2 cm above the eyebrow line (just above the BIS sensor) and palmar left forearm region. The left forearm was not used for drug and fluid infusions, instead, a peripheral venous cannula was placed in this region, and venous blood gas sampling was performed to monitor regional oxygen saturation. In addition to these methods, tissue oxygenation values were observed with left-right cerebral and somatic forearm NIRS sensors. The hemodynamic parameters and arterial and central venous blood gas parameters of the patients were monitored and recorded. Measurement records were made 6 times: T1-5 minutes after anesthesia induction; T2-after the cannulation; T3-at the 10th minute of CPB; T4-10 minutes after cross clamp removal; T5-10 minutes after CPB; T6-upon sternum closing.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 23 (IBM Corp. Armonk, NY, USA). A Kolmogorov-Smirnov test was used to determine whether continuous data were normally distributed or not. Continuous data for the patients in TIVA and SEVO groups were compared using a two-sample *t*-test or Mann-Whitney U test. Differences between two groups according to the nominal data were compared with a chi-square test. Repeated ANOVA was used to analyze repeated measures over time. Power analysis for this study was performed by G*Power 3.1.9.7. Using the repeated ANOVA, statistical power was calculated as 0.99 for $ScvO_2$ based on significance level 0.05, effect size 0.34, partial 0.104 and correlation between repeated measures 0.60 and 0.99 for Forearm NIRS based on significance level 0.05, effect size 0.502, partial 0.201 and correlation between repeated measures 0.30. Significance level was accepted as $p<0.05$ (two-tailed).

Results

A total of 124 adult patients who underwent elective isolated CABG at our tertiary cardiac center were included and 104 of them were analyzed (Figure 1). Demographic data including age, gender, body mass index (BMI), Euroscore II values, and clinical characteristics including the presence of preoperative comorbidities were similar in both groups (Table I). Table I also provides a summary of intraoperative characteristics, such as CPB duration, total operation duration, number of performed anastomoses, and blood product transfusions of the 104 patients in the TIVA (n=52) and SEVO (n=52) groups.

Figure 2 shows the mean values of the forearm NIRS StO_2 of both groups at different times. Forearm NIRS values were higher in the SEVO group compared to the TIVA group throughout the entire study period, but these values were found to be significant only at the 2nd, 3rd, and 6th measurement periods (p=0.029, 0.028, 0.032, respectively). Figure 3 shows the mean values of forearm venous oxygen saturation of both groups, although this value was higher in the SEVO group, there was no statistically significant difference between the groups. In Figure 4, which shows central venous oxygen saturation, in the SEVO group, $ScvO_2$ values were significantly higher in the 2nd, 3rd, and 4th periods, compared to the TIVA group (p=0.019, 0.006, 0.045, respectively). There was no difference between groups in right and left cerebral NIRS values.

The mean arterial pressure, heart rate, temperature, pH, lactate, and hemoglobin values of the groups are given in Table II. In the 5th and 6th periods, mean arterial pressure values in the SEVO group were lower than the TIVA group (p=0.049, 0.032, respectively). Table III contains the postoperative information of both groups of patients. In the SEVO group, extubation time was significantly shorter than in the TIVA group. However, the length of ICU stays, and hospital stay did not differ between the groups. Postop-

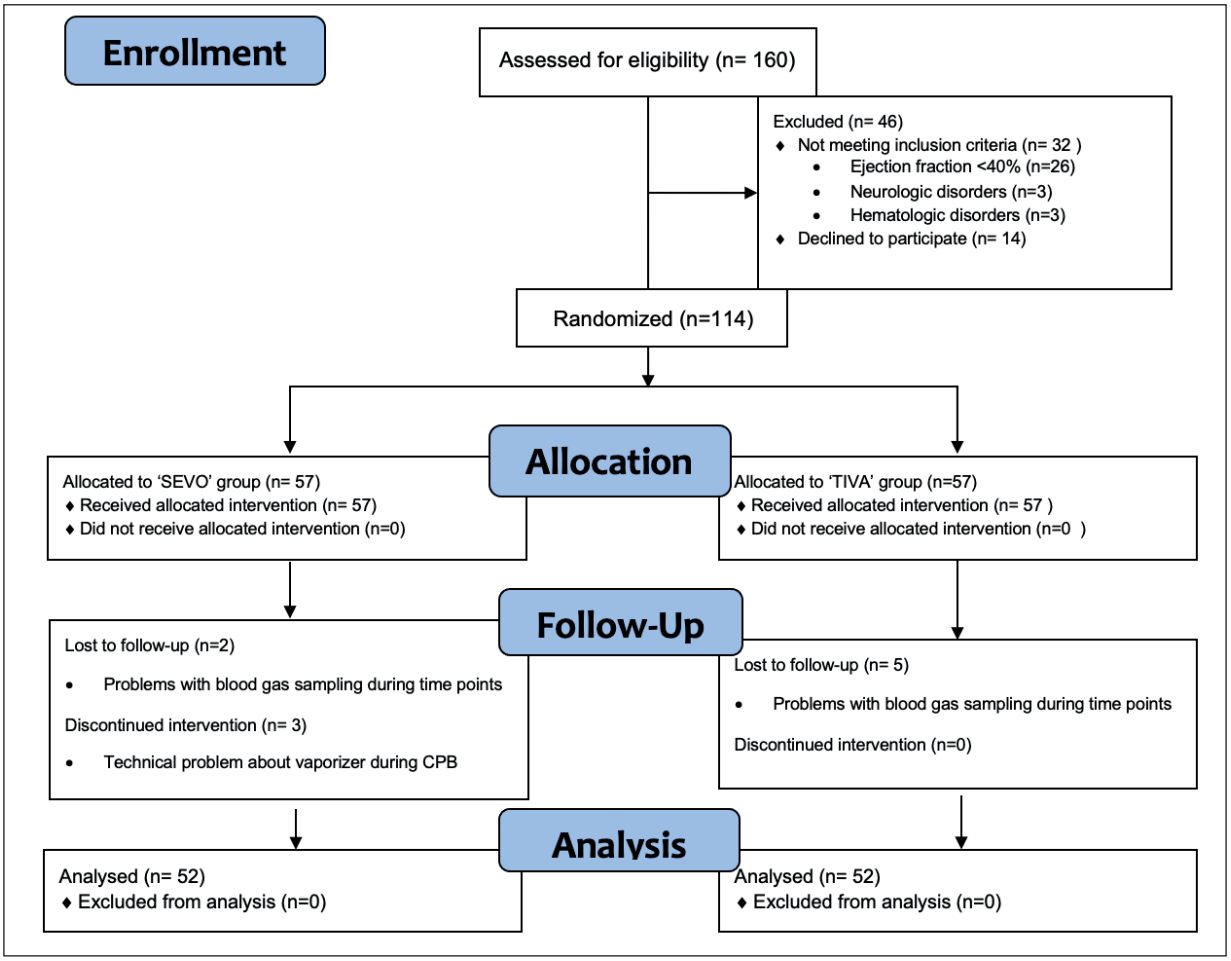

Figure 1. CONSORT flow diagram.

Table I. Preoperative and intraoperative data of the patients in both groups.

	Patients	
Preoperative data	**Group TIVA**	**Group SEVO**
Age (years)	57.87 ± 9.46 (39-79)	59.67 ± 8.03 (32-75)
Body Mass Index (kg.m^{-2})	28.81 ± 3.39 (23.43-39.10)	28.95 ± 3.56 (22.13-40.00)
Euroscore II	0.97 ± 0.37 (0.50-2.19)	1.03 ± 0.83 (0.50-4.87)
Gender (Female:Male) n (%)	10 (9.6): 42 (40.4)	10 (9.6): 42 (40.4)
Hypertension n (%)	36 (34.6)	41 (39.4)
Diabetes mellitus n (%)	21 (20.2)	14 (13.5)
Hyperlipidemia n (%)	31 (30.1)	34 (33.0)
Chronic renal failure n (%)	2 (1.9)	1 (1.0)
Chronic obstructive pulmonary disease n (%)	4 (3.8)	5 (4.8)
Hypothyroidisim n (%)	6 (5.8)	3 (2.9)
Intraoperative data		
Cross clamping duration (min)	60.10 ± 23.67 (18-108)	65.25 ± 28.19 (22-151)
Cardiopulmonary bypass duration (min)	92.17 ± 27.98 (32-144)	98.87 ± 38.21 (33-207)
Total operation duration (min)	279.04 ± 59.96 (110-405)	303.77 ± 86.16 (104-660)
Number of anastomoses (≤ 2, 3, ≥ 4)	19 (18.3), 22 (21.2), 11 (10.6)	16 (15.4), 19 (18.3), 17 (16.3)
Total blood product unit n (%)	14 (13.5)	19 (18.3)
Total urine output (ml)	1239 ± 499 (150-2000)	1142 ± 523 (400-2200)

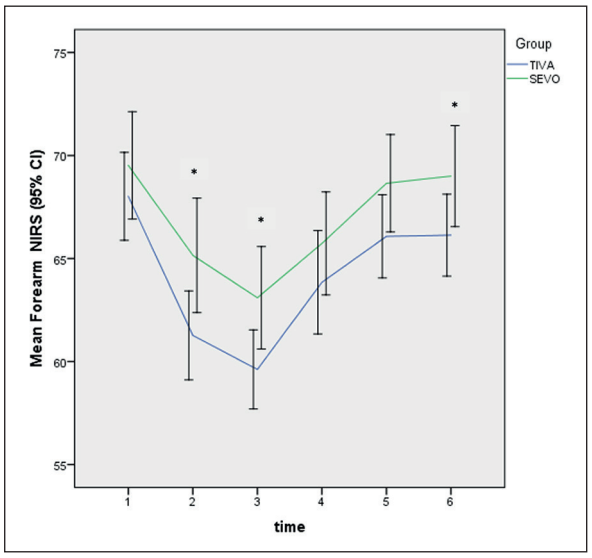

Figure 2. Forearm NIRS values of both groups. *Note:* In the SEVO group, values were found to be significant at the 2nd, 3rd, and 6th measurement periods compared to the TIVA group (p=0.029, 0.028, 0.032, respectively).

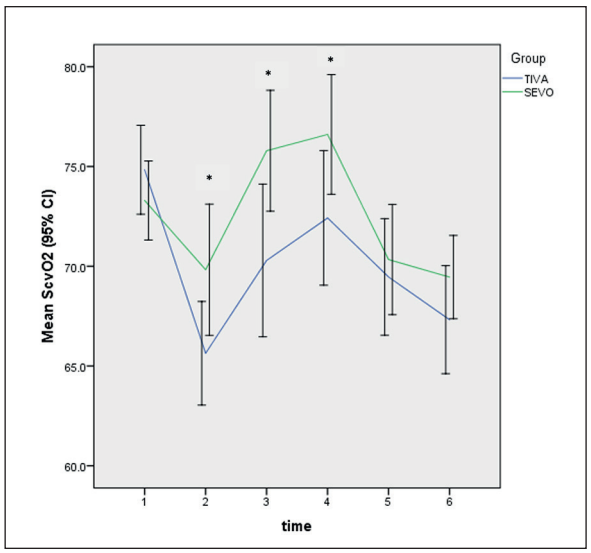

Figure 4. The central venous oxygen saturations of both groups. *Note:* In the SEVO group, $ScvO_2$ values were significantly higher in the 2nd, 3rd, and 4th periods, compared to the TIVA group (p=0.047, 0.026, 0.045, respectively.

erative drainage, blood and blood product use, and postoperative complications were similar between the groups (Table IV).

Discussion

Parallel to improvements in anesthetic methods, efforts are underway to reveal the non-anesthetic effects of medications used in anesthesia, especially those on organ perfusion. In this study, the effects of midazolam-fentanyl based TIVA and sevoflurane-fentanyl based inhalation anesthesia maintenance on intraoperative central and somatic tissue oxygenation parameters were compared in patients undergoing CABG. In tissue oxygenation evaluation, while cerebral NIRS values were found similar, somatic forearm NIRS and $ScvO_2$ values were found to be higher in the SEVO group. Although not significantly different, forearm regional venous oxygen saturation was also higher in the SEVO group.

In clinical practice, monitoring macro-hemodynamic changes is routine, but the detection of microcirculatory changes requires particular effort, as regional tissue oxygenation changes often occur locally and can be observed even when global hemodynamics are normal. Cardiac surgery is associated with significant changes in global cardiovascular dynamics due to the nature of CPB and severely affected tissue perfusion. Further, these global changes in macrocirculation can potentially result in tissue hypoperfusion. During cardiac surgery, microcirculatory perfusion can be severely impaired due to reasons such as decreased cardiac output, non-pulsatile blood flow, activation of inflammation, iatrogenic hemodilution due to CPB, and hypothermia. Studies[3,4] have shown that these changes in mi-

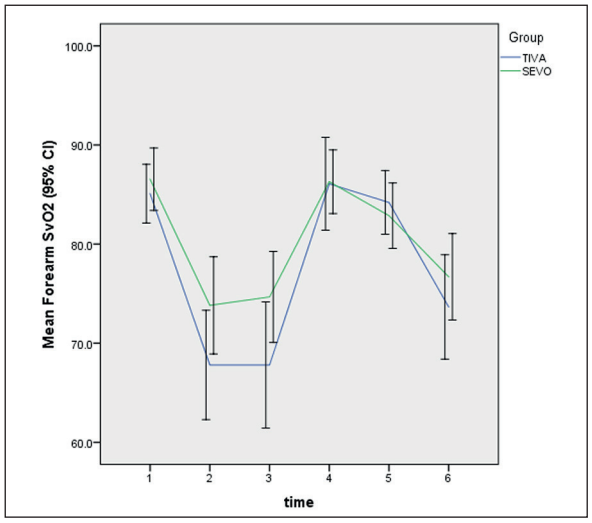

Figure 3. Forearm venous oxygen saturations of both groups. *Note:* There was no statistically significant difference between the groups.

Table II. Intraoperative hemodynamic and blood gas analysis data of the groups.

	Time points	TIVA	SEVO	*p*-value¥		Time points	TIVA	SEVO	*p*-value¥
Mean arterial pressure	1	78.21 ± 12.53	78.36 ± 12.52	0.952	Lactate	1	1.04 ± 0.58	0.93 ± 0.33	0.254
	2	69.08 ± 15.72	67.25 ± 12.57	0.514		2	1.54 ± 1.12	1.53 ± 0.86	0.930
	3	54.98 ± 9.69	54.54 ± 9.44	0.809		3	2.42 ± 1.21	2.65 ± 1.21	0.333
	4	59.98 ± 12.38	59.95 ± 9.40	0.842		4	2.79 ± 1.41	2.86 ± 1.04	0.789
	5	70.09 ± 11.19	66.04 ± 9.49	0.049		5	2.55 ± 1.41	2.53 ± 1.00	0.936
	6	73.03 ± 9.91	68.84 ± 9.71	0.032		6	2.32 ± 1.36	2.40 ± 0.93	0.675
Heart rate	1	68.81 ± 10.04	69.71 ± 10.83	0.660	Hemoglobin	1	13.66 ± 1.58	13.98 ± 1.75	0.125
	2	79.62 ± 19.37	77.17 ± 36.10	0.668		2	12.16 ± 2.36	11.59 ± 2.38	0.632
	3	-	-	-		3	8.49 ± 1.49	8.02 ± 1.38	0.118
	4	80.92 ± 16.98	79.54 ± 14.85	0.659		4	8.73 ± 1.36	8.44 ± 1.68	0.567
	5	89.77 ± 14.14	90.46 ± 16.25	0.817		5	9.32 ± 1.38	9.03 ± 1.47	0.697
	6	90.87 ± 15.29	88.62 ± 15.00	0.451		6	9.62 ± 1.54	9.22 ± 1.59	0.248
Temperature °C	1	36.22 ± 0.35	36.27 ± 0.62	0.611	Arterial pH	1	7.39 ± 0.05	7.38 ± 0.04	0.511
	2	34.96 ± 0.59	34.86 ± 0.83	0.498		2	7.38 ± 0.06	7.38 ± 0.06	0.843
	3	32.11 ± 1.12	32.08 ± 0.77	0.855		3	7.36 ± 0.05	7.36 ± 0.04	0.680
	4	35.58 ± .1.82	35.45 ± 1.48	0.700		4	7.32 ± 0.97	7.35 ± 0.06	0.387
	5	36.66 ± 0.54	36.57 ± 1.20	0.621		5	7.35 ± 0.05	7.34 ± 0.04	0.099
	6	36.41 ± 0.56	36.48 ± 0.55	0.550		6	7.36 ± 0.05	7.34 ± 0.05	0.087
Central venous pH	1	7.36 ± 0.04	7.17 ± 1.05	0.177	Venous pH	1	7.37 ± 0.05	7.36 ± 0.05	0.914
	2	7.33 ± 0.06	7.34 ± 0.05	0.350		2	7.33 ± 0.07	7.36 ± 0.09	0.094
	3	7.32 ± 0.05	7.32 ± 0.05	0.715		3	7.33 ± 0.08	7.34 ± 0.06	0.320
	4	7.34 ± 0.05	7.32 ± 0.04	0.320		4	7.35 ± 0.08	7.33 ± 0.06	0.094
	5	7.32 ± 0.08	7.31 ± 0.05	0.448		5	7.35 ± 0.07	7.33 ± 0.05	0.167
	6	7.32 ± 0.05	7.30 ± 0.05	0.080		6	7.33 ± 0.09	7.32 ± 0.06	0.320
$ScvO_2$	1	74.84 ± 8.00	73.30 ± 7.11	0.303	Forearm	1	68.02 ± 7.67	69.52 ± 9.37	0.374
	2	65.64 ± 9.32	69.83 ± 11.81	0.047	NIRS	2	61.27 ± 7.75	65.15 ± 9.97	0.029
	3	70.29 ± 13.74	75.79 ± 10.88	0.026		3	59.62 ± 6.89	63.10 ± 8.95	0.028
	4	71.42 ± 12.12	76.61 ± 10.77	0.045		4	63.85 ± 9.00	65.73 ± 8.77	0.287
	5	69.46 ± 10.48	70.34 ± 9.92	0.664		5	66.08 ± 7.26	68.65 ± 8.50	0.099
	6	67.32 ± 9.72	69.46 ± 7.50	0.212		6	66.13 ± 7.15	69.00 ± 8.80	0.032
Cerebral NIRS Left	1	61.23 ± 8.35	60.56 ± 9.62	0.704	Cerebral NIRS Right	1	61.62 ± 8.19	61.21 ± 8.22	0.802
	2	55.77 ± 11.36	56.23 ± 12.51	0.433		2	56.67 ± 10.79	56.87 ± 10.37	0.922
	3	50.46 ± 8.59	51.81 ± 11.49	0.500		3	52.19 ± 8.97	51.67 ± 9.81	0.779
	4	55.90 ± 10.44	55.31 ± 8.68	0.752		4	57.31 ± 10.14	55.98 ± 8.54	0.472
	5	56.17 ± 9.92	57.83 ± 9.01	0.376		5	57.87 ± 8.08	58.60 ± 9.05	0.665
	6	57.25 ± 8.01	57.33 ± 8.61	0.962		6	58.29 ± 7.87	58.23 ± 8.82	0.767

¥: Two- samples *t*-test, $ScvO_2$: Central venous oxygen saturation, NIRS: Near-infrared spectroscopy. In Table II presenting descriptive statistics (mean ± SD) and p-values from the results of two-samples *t*-test, there was a statistically significant difference in mean interest between TIVA and SEVO groups in mean arterial pressure at the 5th and 6th time points (p = 0.049, 0.032, respectively), in central venous oxygen saturation ($ScvO_2$) at 2nd ,3rd and 4th time points (p = 0.047, 0.026, 0.045, respectively), in Forearm NIRS StO_2 at the 2nd, 3rd and 6th time points (p = 0.029, 0.028, 0.032 respectively).

crovascular circulation during CPB are observed with a significant reduction in the proportion of perfused vessels and medium vessel microvascular flow index (MFI). Although CPB has been cited as the cause of microvascular changes, there is also a study[5] that objects to this, claiming that these changes occurred before CPB. This final study suggested that the MFI in small vessels began to deteriorate earlier than the commencement of CPB, and that the induction of anesthesia was responsible for this deterioration.

Aside from discussions about when exactly the deterioration in the microvascular bed begins during cardiac surgery, there are also studies[3,4,6,7] describing when this deterioration resolves. They propose differing opinions about when changes in the microvascular system return to normal. It has been found that functional capillary density was moderately reduced during CPB and recovered to its initial value one hour after reperfusion[6]. Other articles[3,4,7] suggested that this improved in the early postoperative period, and still

Table III. Pairwise Comparisons of TIVA and SEVO groups for $ScvO_2$ and Forearm NIRS variables.

Measure	Group	Group	Mean difference	95% Confidence interval for difference¥	
				Lower bound	Upper bound
$ScvO_2$	TIVA	SEVO	-2.557*	-5.055	-0.059
	SEVO	TIVA	2.557*	0.059	5.055
Forearm NIRS	TIVA	SEVO	-2.699*	-5.242	-0.155
	SEVO	TIVA	2.699*	0.155	5.242

$ScvO_2$: Central venous oxygen saturation, NIRS: Near-infrared spectroscopy. ¥: repeated ANOVA, *: $p < 0.05$. Pairwise comparisons were then used for all variables to investigate whether there was a difference in measures between TIVA and SEVO groups. In Table III, the results of repeated ANOVA were given only for variables having statistically significant mean differences ($p < 0.05$). TIVA and SEVO groups were statistically significantly different from each other only for $ScvO_2$ and Forearm NIRS variables ($p < 0.05$). Table III shows that measures in both $ScvO_2$ and Forearm NIRS variables for SEVO group of subjects are higher than those for TIVA group of subjects.

others claimed that this could take up to 24 hours. In our study, microcirculatory blood flow was not measured, but regional tissue perfusion that indirectly reflected this was evaluated and it was observed that forearm NIRS and venous oxygen saturation decreased during the cannulation and CPB periods in patients who underwent coronary surgery regardless of the type of anesthesia. Although this decline gradually improved towards the end of the surgery, it did not completely return to basal values during sternum closure.

The relationship between tissue oxygenation changes and anesthesia maintenance in cardiac surgery is the focus of this study. In cardiac surgery, the fondness for inhalation agents and especially sevoflurane has increased greatly since the discovery that its preconditioning effect provides myocardial protection. On the other hand, a special vaporizer is needed to deliver an inhalation agent during CPB, so cardiac anesthesiologists may either go directly to TIVA methods or, if they use inhalation methods, perform TIVA during CPB.

In our clinic, midazolam-fentanyl-based anesthesia is a standard technique that has been used for many years and is still in use. Many different combinations have been studied in the literature for both inhalation and TIVA techniques. We applied midazolam-fentanyl-based anesthesia in the TIVA group of our study in order to observe the results of the method we applied in our own practice. In the inhalation group, we combined sevoflurane, which we can also apply during CPB, with fentanyl. While the inhalation agent was administered continuously, midazolam was administered intermittently in the TIVA group.

Table IV. Postoperative data of the patients in both groups.

Preoperative data	Patients		
	Group TIVA	Group SEVO	*p*-value
Extubation time(h)	9.58 ± 5.39 (5-38)	7.95 ± 4.66 (4-28)	0.004þ*
Length of intensive care unit stay(d)	1.37 ± 0.89 (1-6)	1.43 ± 0.94 (1-5)	0.748þ
Length of hospital stay(d)	5.44 ± 2.57 (2-16)	5.35 ± 1.99 (0-12)	0.501þ
Postoperative inotropic using n (%)	5 (4.8)	4 (3.8)	0.647¥
Postoperative blood products transfusions n (%)	20 (19.2)	16 (15.4)	0.537¥
Postoperative drainage (ml)	645 ± 326 (0-2200)	667 ± 363 (150-2000)	0.542þ
Postoperative atrial fibrillation n (%)	3 (2.9)	2 (1.9)	1.000¥
Postoperative revision n (%)	2 (1.9)	4 (3.8)	0.678¥
Postoperative pneumonia n (%)	1 (1.0)	1 (1.0)	1.000¥
Postoperative neurological events n (%)	2 (1.9)	1 (1.0)	1.000¥
Postoperative complications n (%)	7 (6.7)	8 (7.7)	1.000¥
Mortality within 30 days n (%)	0 (0.0)	1 (1.0)	1.000¥

*: $p < 0.05$; þ: Mann-Whitney test; ¥: Chi-Square test.

The maintenance dose of midazolam was adjusted and administered once every 30-45 minutes according to the patients' weight and BIS values. Continuous infusion of midazolam and fentanyl could produce a more stable drug plasma level. However, in cardiac surgery, many factors such as hemodilution, intraoperative autologous blood donation, drug absorption and sequestration from the cardiopulmonary bypass circuit, changing serum drug carriers albumin-globulin levels, hypothermia, rewarming, and transfusions may cause fluctuations in plasma drug levels.

Tissue perfusion and oxygenation disturbances were found in different surgical settings despite the optimization of systemic macro-hemodynamic parameters[8], and this dysfunction was associated with the development of postoperative complications[9]. It was shown that in patients undergoing open abdominal aortic aneurysm repair, microvascular perfusion and somatic tissue oxygenation were generally preserved. However, the use of inhalation anaesthesia was associated with increased microvascular density and reactivity, while these remained unaltered with TIVA[10]. The adverse effects of midazolam on regional tissue perfusion led to microcirculatory derangements even in non-septic situations[11]. Inhalation anesthetics, for their part, cause peripheral vasodilation and reduce vascular permeability, thereby promoting local microvascular recruitment and tissue oxygen diffusion[12,13]. In the MYRIAD trial including patients undergoing elective, isolated CABG, intraoperative anesthesia with an inhalational anesthetic did not result in a significantly lower number of deaths at one year than TIVA[14]. In this study, however, one third of the cases were off-pump cardiac surgery, and patients who were administered the diverse inhalation agents sevoflurane, isoflurane, and desflurane were all evaluated as one group, while those administered propofol and midazolam constituted the TIVA group. The grouping, however, of such powerful and diverse drugs in each group represents a serious limitation of the study. Inhalation agents and intravenous agents both have separate effects on organ functions. It is the co-administration of propofol during anesthesia induction which has been shown to reduce the potential preconditioning effect of inhalational anesthetics[15]. Some scholars[16], however, suggest that myocardial protection can actually be enhanced by combination therapy with propofol. In most of the studies[13,15] in the literature, propofol is used in TIVA groups. However, propofol is a unique medicine, and we believe it would be more accurate to examine its effects in an entirely isolated manner. A similar situation applies to remifentanil, which is peculiar among opioids. It has been suggested that opioids could have a preconditioning cardioprotective effect that would potentially mask the effect of volatile agents. However, cardioprotective doses of opioids are much higher than the doses used for anesthesia in clinical practice. In light of this information, there are few studies[10-14] examining the effect of anesthetic medicine management on tissue perfusion and oxygenation, and this makes our results valuable.

Cerebral and somatic near-infrared spectroscopy monitors are commonly used to detect tissue hypoperfusion and oxygenation in various circumstances. The organism's first response in critical situations is to divert blood flow to the brain from peripheral tissues that are more resistant to hypoperfusion. Therefore, monitoring the brain in terms of detecting the presence of a critical condition may cause a delay. Certainly, we should monitor the brain in terms of ischemia and hypoperfusion, but more effective holistic hypoperfusion monitoring can be performed if somatic muscle tissue is also monitored together. It has been demonstrated that the NIRS technique is well suited for the non-invasive evaluation of limb perfusion[17]. Physiologically, the forearm is a suitable limb site for peripheral NIRS measurement, as it is an early and dominant vasoconstriction site in cases of circulatory distress[18,19]. Placing a NIRS sensor parallel to the proximal forearm over the antebrachial muscle ensures a stable sensor position. A study[20] using somatic muscle NIRS to investigate the microcirculatory effect of general anesthetics showed that general anesthesia with remifentanil-propofol and remifentanil-sevoflurane caused marked changes in skeletal muscle microcirculation. It was observed that while muscle blood flow increased with remifentanil-propofol, microvascular compliance and muscle oxygen consumption decreased in those treated with remifentanil-sevoflurane[20]. Advances in the use of near-infrared technology in cardiac surgery further reveal the understanding of light propagation in tissues that enables accurate assessment of changes in regional tissue oxygenation and blood flow. These parameters can provide valuable insight into the underlying mechanisms that regulate O_2 transport and tissue O_2 utilization in microcirculation.

Although both midazolam and fentanyl have a rapid onset and short clinical effect time in single doses, after continuous administration,

accumulation occurs, and long-term sedative effects can be observed[21]. In our study, extubation time was significantly shorter in the SEVO group. However, ICU and hospital stay were not different between the groups. The fact that the duration of stay in the intensive care unit is not different between the groups may be related to the surgeons' desire for caution, keeping the patients who do not require intensive care in the intensive care unit.

Conclusions

In our study, in which two different anesthesia management regimens were compared in patients admitted to CABG operations, cerebral NIRS values were found to be similar in the groups, possibly due to the cerebral autoregulation effect. However, due to higher somatic forearm NIRS and $ScvO_2$ values in patients using the SEVO-based regimen, it was concluded that sevoflurane-based inhalation anesthesia maintenance provides better intraoperative central and somatic tissue oxygenation parameters in coronary surgery.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Authors' Contribution

Conception and design of the study: Hülya Yiğit Özay, Aslı Demir, Eda Balcı, Melike Bahçecitapar, Ayşegül Özgök; acquisition of data: Hülya Yiğit Özay, Eda Balcı; analysis and interpretation of data: Melike Bahçecitapar; drafting the article: Hülya Yiğit Özay, Aslı Demir; making critical revisions related to relevant intellectual content of the manuscript: Eda Balcı, Melike Bahçecitapar, Ayşegül Özgök; supervision: Aslı Demir; validation and final approval of the version of the article to be published: Hülya Yiğit Özay, Aslı Demir, Eda Balcı, Melike Bahçecitapar, Ayşegül Özgök.

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Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Trial Registration Number

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