

# Optic Nerve Sheath Diameter Changes During Laparoscopic Cholecystectomy in the Reverse Trendelenburg Position: Total Intravenous Anesthesia vs. Desflurane

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## What is known on this subject?

Sonographically determined optic nerve sheath diameter (ONSD) has been proposed as a straightforward and non-invasive technique for detecting elevated intracranial pressure (ICP). Several studies have measured ONSD in different positions by comparing other anesthesia methods. However, studies on the reverse Trendelenburg position are limited.

## What this study adds?

Ultrasonographically assessed ONSD as a representative metric for ICP is evaluated to assess the effects of desflurane and propofol-based total intravenous anesthesia in patients undergoing elective laparoscopic procedures in the reverse Trendelenburg position.

## ABSTRACT

**Objective:** We aimed to compare the impacts of total intravenous anesthesia (TIVA) and desflurane on optic nerve sheath diameter (ONSD) among patients undergoing elective laparoscopic surgery in the reverse Trendelenburg position.

**Material and Methods:** In this prospective randomized trial, individuals aged 18 to 65 scheduled for laparoscopic cholecystectomy were recruited and randomly divided into either the TIVA or desflurane group. ONSD was assessed at four distinct time points: before anesthesia administration (T0), 5 min after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 min after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). The primary outcome was the mean ONSD measurement at each of these time points within the TIVA and desflurane groups throughout the surgery.

**Results:** No statistical difference was found in the mean ONSD values between the groups at all four points. However, the mean change in ONSD between T0 and T1 points and T1 and T2 points was significantly lower in the TIVA group ( $p=0.025$ ,  $p=0.006$ , respectively) than in the desflurane group.

**Conclusion:** Our findings imply that TIVA may be more appropriate for patients undergoing surgery in the reverse Trendelenburg position because of minor changes in ONSD.

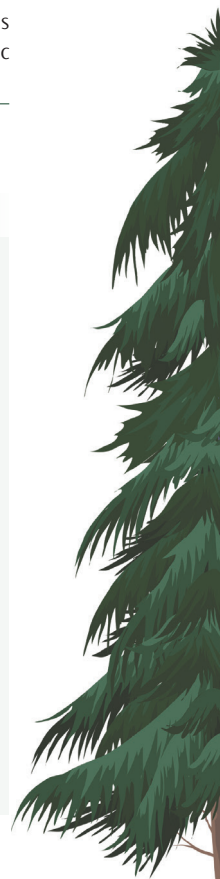
**Keywords:** Ultrasonography, reverse trendelenburg position, pneumoperitoneum, optic nerve sheath diameter

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## Introduction

Laparoscopic surgery has gained popularity as the preferred approach for numerous treatments recently (1). Nevertheless, laparoscopic procedures necessitate the creation of an artificial pneumoperitoneum, which might result in physiological alterations such as an increase in intracranial pressure (ICP) (2). While laparoscopy might lead to a major negative impact on cerebrovascular condition due to increased ICP, the ideal approach for monitoring ICP, which is invasive, has a risk of serious complications such as bleeding or infection (3). Sonographically measured optic nerve sheath diameter (ONSD) has been proposed as a straightforward and non-invasive technique for detecting elevated ICP (3,4).

Total intravenous anesthesia (TIVA) is commonly acknowledged for its capacity to lower ICP by diminishing both cerebral blood flow (CBF) and cerebral blood volume (CBV) (5). In contrast, inhalational anesthetics have a dose-dependent effect of increasing CBF by stimulating cerebral vasodilatation, which in turn may lead to an increase in ICP (6,7,8). Moreover, the patients' positions are changed to ease the surgical technique, which also affects ICP. Several studies have measured ONSD in different positions by comparing other anesthesia methods (9,10,11,12,13,14,15). However, studies on the reverse Trendelenburg position are limited (11). To the best of our knowledge, no study has compared ONSD measurements between desflurane and TIVA administration in the reverse Trendelenburg position.

Ultrasonographically assessed ONSD as a representative metric for ICP was evaluated to assess the effects of desflurane- and propofol-based TIVA in patients undergoing elective laparoscopic procedures in the reverse Trendelenburg position.

## Material and Methods

### Participants

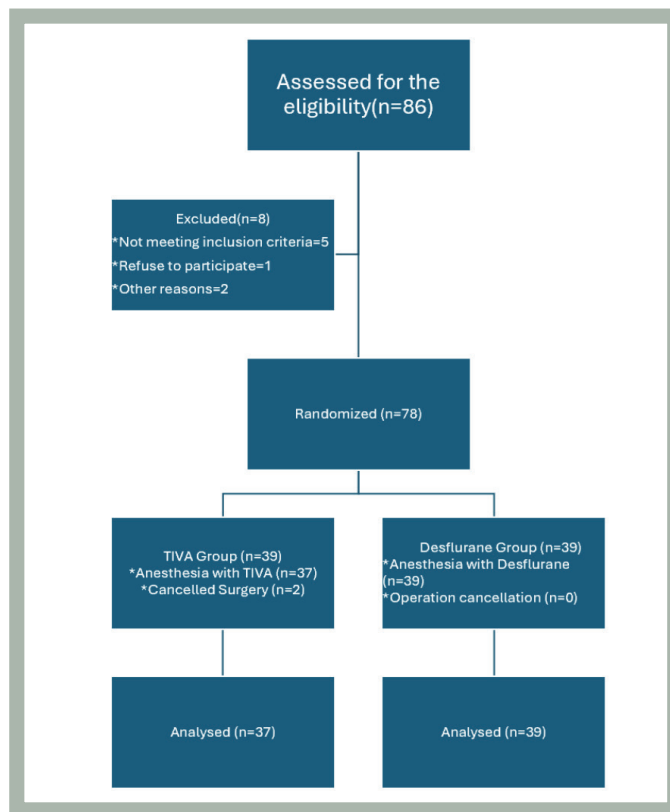
This prospective randomized controlled trial was conducted at University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital following approval from the Ethics Committee of the University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital (approval number: 2019/514/148/19, date: 27/02/2019). All participants provided written informed consent. This study adhered to the ethical principles outlined in the Declaration of Helsinki-2013 and followed guidelines for good clinical practice.

Between March and July 2019, a total of eighty-six patients, classified as American Society of Anesthesiologists (ASA) class I to II and aged between 18 and 65 years, were enrolled in the study. Two patients with previous cerebrovascular incidence with hydrocephalus and intracranial hemorrhage, two patients with glaucoma, one patient with body mass index >30, one patient who refused to participate, and two patients due to other reasons were excluded from enrollment.

Anesthesiologist randomly assigned patients to the desflurane or TIVA groups 1 h before surgery. After randomization, participants were divided into two groups: desflurane group, which received desflurane inhalation and remifentanyl infusion (n=39); and TIVA group, which received propofol and remifentanyl infusion for anesthesia maintenance during surgery (n=39). Two patients in the TIVA group were excluded due to operation cancelation (Figure 1).

### Anesthetic and Surgical Techniques

In the operating room, patients were monitored using pulse oximetry, electrocardiography, and non-invasive blood pressure monitors. Following 3 min of preoxygenation, patients in the desflurane group received 2 mg/kg of propofol for anesthesia induction, followed by maintenance with 4-6% desflurane and 0.05-0.15 mcg/kg/min IV remifentanyl. Patients



**Figure 1.** Consort flow diagram

TIVA: Total intravenous anesthesia

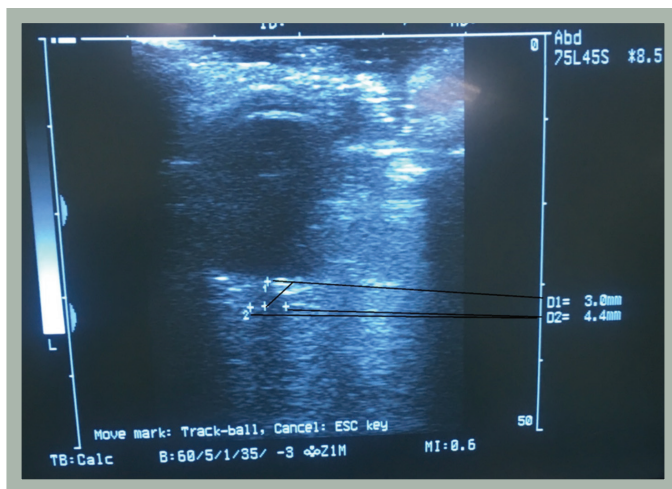
in the TIVA group received continuous infusions of propofol and remifentanyl via a target-controlled infusion pump. Propofol dosage was adjusted within a range of 2-5 mcg/mL, whereas remifentanyl dosage was adjusted within a range of 2-5 ng/mL. Both groups received 0.6 mg/kg of rocuronium for muscle relaxation followed by intubation. Mechanical ventilation was maintained in a volume-controlled mode with a tidal volume of 6 mL per kilogram of ideal body weight.

The respiratory rate was adjusted to maintain  $SpO_2$  between 97-100% and end-tidal carbon dioxide ( $etCO_2$ ) partial pressure at  $35 \pm 5$  mmHg. Positive end-expiratory pressure (PEEP) was maintained between 3 and 5  $cmH_2O$ . All patients were kept normothermic, and their depth of anesthesia was monitored using a bispectral index score monitor set at 40-60 to ensure comparable levels of anesthesia between the two groups. Throughout the procedure, carbon dioxide pneumoperitoneum was maintained at an intra-abdominal pressure of  $15 \pm 5$  mmHg in patients positioned in the reverse Trendelenburg position.

No patients were excluded from the study because of a lack of experiencing unstable vital signs, change into open abdominal surgery, or technical challenges of measurement of ONSD.

### Measurements

An experienced anesthesiologist, unaware of the patient's group, used a 7.5-MHz linear probe to evaluate ONSD using ultrasonography. After applying ultrasonic gel, the linear probe was positioned and affixed onto the patient's closed eyelids using transparent Tegaderm. The optic disk vitreous body, and hypoechoic ONS were examined by carefully adjusting the angle of the probe (Figure 2). The ONSD was



**Figure 2.** D1: Distance behind the eyeball, D2: ONSD  
ONSD: Optic nerve sheath diameter

measured vertically 3 mm posterior to the optic disk in both eyes' sagittal and transverse planes using electronic calipers. For analysis, the mean of the four measurements was used. Each measurement was completed within a 1-min timeframe. Four measurements were taken at specific time points: before anesthesia administration (T0), 5 min after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 min after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3).  $EtCO_2$ , mean arterial pressure (MAP), heart rate, and peak airway pressure (PAP) were systematically monitored and recorded at each of the four specified time intervals.

The primary outcome was the measurement of mean ONSD at each observed time point in the TIVA and desflurane groups during surgery. The secondary outcome was the calculation of changes in mean ONSD and diameter trends in the observed time in the two groups.

We hypothesize that ONSD significantly increases due to the pneumoperitoneum effect, and that TIVA results in a lesser increase in ONSD compared with desflurane anesthesia.

### Statistical Analysis

A previous study documented a mean ONSD of 4.7 mm and a maximum ONSD value of 5.1 mm in patients receiving volatile anesthetics (8). According to this study, detecting a mean difference in ONSD between two independent groups with a type I error of 0.05, a power of 80%, and an effect size of 0.6 necessitated a sample size of 36 patients per group.

The normality of continuous data was assessed using the Shapiro-Wilk test. Continuous data are presented as mean  $\pm$  standard deviation or median (interquartile range), whereas categorical data are presented as frequency (%). Data were compared using independent two-sample t-tests, Mann-Whitney U tests, chi-square tests, or Fisher's exact tests as appropriate. A p value  $<0.05$  was considered statistically significant.

Changes in ONSD over time were evaluated using repeated measures ANOVA with Bonferroni correction, where an adjusted p value of 0.0125 was considered statistically significant in post-hoc tests. All analyses were conducted using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA).

## Results

Seventy-six patients in the two groups were analyzed; the median age, height, and weight were similar. There were more women than men in both groups, and the number of

ASA-II patients was higher than that of ASA-I patients in both groups, but no significant difference was detected between the groups. The number of patients with hypertension was similar, whereas the number of patients with diabetes was higher in the TIVA group, but no significant difference was found. The duration of operation and anesthesia were similar in both groups (Table 1).

The ONSD measurements were similar in the two groups; no statistical difference was detected in any of the four measurements. The sheath diameter changes between T0 and T1 points and between T1 and T2 points were

significantly lower in the TIVA group than in the desflurane group ( $p=0.025$ ,  $p=0.006$ , respectively). Other measurement differences between observation points were similar in both groups, and no statistically significant difference was detected (Table 2).

When the groups were evaluated independently, a significant increase in ONSD was found between T0 and T1 points, a substantial decrease between T1 and T2 points, and between T1 and T3 points in both groups separately, whereas no significant difference was found in other comparisons ( $p<0.00$ ,  $p<0.001$ ,  $p<0.001$ , respectively) (Figure 3).

**Table 1. Characteristics of the patients**

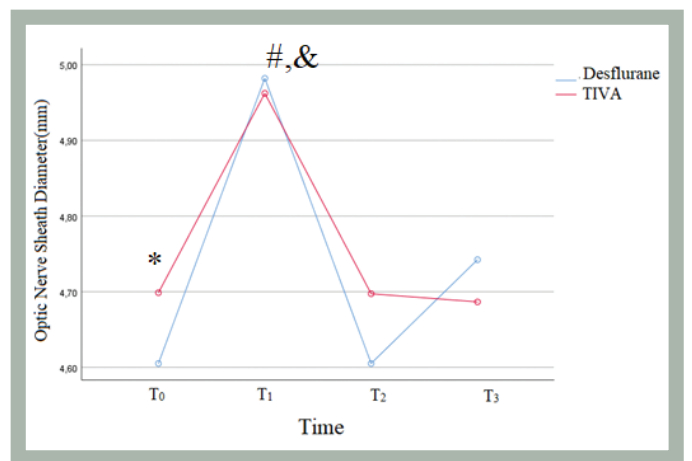
Variables	TIVA group (n=37)	Desflurane group (n=39)	p value
Age (years)	55 (53-61.5)	54.7 (49-57)	0.075
Height (cm)	162.8 (157-169)	164 (158-170)	0.544
Weight (kg)	76 (71-81.3)	77.3 (70.6-82)	0.317
Gender (male/female)	8 (10.5%)/29 (38.2%)	13 (17.1%)/26 (34.2%)	0.376
<b>ASA</b>			
ASA-I	11 (14.5%)	10 (13.2%)	0.887
ASA-II	26 (34.2%)	29 (38.2%)	
Hypertension	13 (17.1%)	14 (18.4%)	0.945
Diabetes mellitus	14 (18.4%)	9 (11.8%)	0.250
Duration of operation (min)	35 (22.5-35)	35 (25-35)	0.991
Duration of anesthesia (min)	45 (32.5-45)	45 (35-45)	0.991

Data are shown as median (IQR) or number (% , frequency). IQR: Interquartile range, TIVA: Total intravenous anesthesia, ASA: American Society of Anesthesiologists

**Table 2. Comparison of mean ONSD values and changes between the two groups**

Variables	TIVA group (n=37)	Desflurane group (n=39)	p
ONSD T0 (mm)	4.7±0.4	4.6±0.33	0.208
ONSD T1 (mm)	4.96±0.33	4.98±0.41	0.811
ONSD T2 (mm)	4.7±0.35	4.6±0.4	0.58
ONSD T3 (mm)	4.68±0.37	4.74±0.4	0.883
<b>ONSD difference</b>			
T0-T1 (mm)	0.31±0.24	0.46±0.31	<b>0.025</b>
T1-T2 (mm)	0.35±0.22	0.40±0.32	<b>0.006</b>
T2-T3 (mm)	0.20±0.19	0.24±0.16	0.466

Data are shown as mean ± standard deviation. Before anesthesia administration (T0), 5 minutes after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 minutes after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). TIVA: Total intravenous anesthesia, ONSD: Optic nerve sheath diameter



**Figure 3.** Linear mean ONSD trend of Desflurane and TIVA groups T<sub>0</sub>: Before anesthesia administration, T<sub>1</sub>: 5 minutes after carbon dioxide insufflation in the reverse Trendelenburg position, T<sub>2</sub>: 5 minutes after the termination of pneumoperitoneum in the reverse Trendelenburg position, T<sub>3</sub>: After extubation, ONSD: Optic nerve sheath diameter, TIVA: Total intravenous anesthesia

\*: Mean difference between T<sub>0</sub> and T<sub>1</sub>,  $p<0.001$

#: Mean difference between T<sub>1</sub> and T<sub>2</sub>,  $p<0.001$

&: Mean difference between T<sub>1</sub> and T<sub>3</sub>,  $p<0.001$



The MAP measurements were higher in the TIVA group at time T0, higher in the desflurane group at time T1, and similar in both groups at T2 and T3. However, no statistically significant difference was observed. The value of EtCO<sub>2</sub> was higher in the TIVA group at all three time points. However, at T2, the difference between the TIVA and desflurane groups was statistically significant (p=0.02). PAP was equal in both groups at T1, higher in the desflurane group at T2, and higher in the TIVA group at T3, and no statistically significant difference was found for all three measurements (Table 3).

## Discussion

Our study revealed significantly less sheath diameter change in the TIVA group. In addition, for the values measured at different time points during follow-up, as expected, there was an increase in the mean ONSD value with insufflation, followed by a decrease and return to baseline values. At the termination of the pneumoperitoneum, the observed value of EtCO<sub>2</sub> was higher in the TIVA group, which was an unexpected result.

This study assessed the differences in the mean ONSD measurements of the TIVA and desflurane groups during laparoscopic cholecystectomy. In contrast to our hypothesis, we found no significant variations in ONSD measurements between the two groups. These findings contrasted from the results of the study conducted during robot-assisted laparoscopic prostatectomy. Which revealed significantly lower ONSD measurements during propofol anesthesia

compared with sevoflurane anesthesia 60 min after pneumoperitoneum and the Trendelenburg position (9).

Farling et al. (10) indicated a significant decrease in ICP after 2 hours of continuous propofol administration in head-injured patients. However, in our study, the surgical duration was less than 2 hours for all cases. Even if there was less change in ONSD in the TIVA group, this might be the reason for not seeing the ONSD decreasing effect of propofol and finding similar measurements between the desflurane and TIVA groups. Another reason for the similar measurements could be the preventive effect of the reverse trendelenburg position in ICP increase.

Demirgan et al. (11) stated that adopting the reverse Trendelenburg position before pneumoperitoneum prevented an increase in ONSD. These results slightly differ from one animal study that showed the reverse Trendelenburg position does not counteract the elevation in ICP observed with insufflation (12). Sahay et al. (2) noted that placing patients' heads down or heads up after pneumoperitoneum significantly increased their ICPs, although this increase was less for patients placed in reverse Trendelenburg position. However, we could not observe whether reverse trendelenburg had any preventive effect because the positioning of the patient and intra-abdominal pressure were standardized in our study.

The average ONSD value remained below 5 mm in both groups, indicating that increased ICP may be excluded as a possibility. Intracranial hypertension is characterized by an ICP exceeding 20 mmHg (13). In a prior study, Tayal et al. (14) demonstrated that an ONSD of 5.00 mm correlated with computed tomography findings indicative of elevated ICP. They also reported a sensitivity of 100% for an ONSD of 5 mm in predicting an ICP exceeding 20 mmHg.

The result of lower changes in mean ONSD in the TIVA group during the insufflation and termination of carbon dioxide correlated with the study that TIVA is more effective than inhalation of sevoflurane in reducing the rise in ICP and preserving cerebral autoregulation (15). Additionally, the research of Petersen et al. (6) showed the significantly higher carbon dioxide reactivity observed during anesthesia with volatile agents may elucidate the higher change observed in the desflurane group. After the end of the pneumoperitoneum period, ONSD measurements returned to the basal values, which showed the reversible effect of CO<sub>2</sub> insufflation.

In our study, the degree of reverse trendelenburg and hemodynamics of the patients were kept constant throughout. The MAP and PAP were comparable. Different ventilation modes have been observed to affect oxygenation and ventilation during laparoscopic procedures, consequently

**Table 3. Comparison of mean arterial pressure, end-tidal CO<sub>2</sub>, and peak airway pressure between two groups**

Variables	TIVA group (n=37)	Desflurane group (n=39)	p
MAP T0 (mmHg)	113±16	110±13	0.087
MAP T1 (mmHg)	97±17	98±22	0.067
MAP T2 (mmHg)	93±16	93±13	0.416
MAP T3 (mmHg)	101±14	101±13	0.465
EtCO <sub>2</sub> T1 (mmHg)	33±4	31±3	0.109
EtCO <sub>2</sub> T2 (mmHg)	35±4	34±3	<b>0.02</b>
EtCO <sub>2</sub> T3 (mmHg)	34±5	32±3	0.097
Peak T1 (cmH <sub>2</sub> O)	24±4	24±4	0.287
Peak T2 (cmH <sub>2</sub> O)	19±4	20±4	0.083
Peak T3 (cmH <sub>2</sub> O)	21±5	20±5	0.793

Data are shown as mean ± standard deviation. Before anesthesia administration (T0), 5 minutes after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 minutes after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). MAP: Mean arterial pressure, TIVA: Total intravenous anesthesia

influencing ICP through the aforementioned mechanisms. Therefore, we monitored these factors, and to minimize bias, we adjusted the respiration rate to maintain EtCO<sub>2</sub> of 35±5 mmHg. PEEP values were maintained between 3 and 5 cmH<sub>2</sub>O to minimize the airway pressure difference between individuals, which finally affected the intrathoracic pressure and ICP. We observed significantly higher EtCO<sub>2</sub> values in the TIVA group at just one observation period, which could be explained by the decreased carbon dioxide reactivity with propofol-based anesthesia (6).

### Study Limitations

The intra- and interobserver variation in the measurement of ONSD might have been observed in our study as a limitation. To mitigate this bias, we enlisted a single experienced anesthesiologist to conduct the measurements four times, averaging the results each time. We measured ONSD before induction and 5 min after carbon dioxide insufflation and positioning. Because of the short operation time and technical necessities, we could not observe the effect of anesthetic agents and the impact of pneumoperitoneum alone without the position. When the human brain detects increases in ICP, compensatory mechanisms are activated. The Monroe-Kellie doctrine upholds the dynamic equilibrium among arterial and venous blood, parenchymal tissue, and cerebrospinal fluid, which is essential for preserving cerebral autoregulation and averting an elevation in ICP. This concept might elucidate the observation that none of the patients in either group exhibited ONSD values exceeding the mean value of 5.0 mm, which is another limitation of this study. Similarly, the short operation time and relatively healthy (ASA I-II) patient group also limited the evaluation of possible compensatory mechanisms in ICP. According to the exclusion criteria, patients enrolled in our study did not present with any pre-existing cerebral disease. Therefore, this study did not evaluate the effect of ICP on individuals with cerebral disease. Patients with pre-existing cerebral ischemia or elevated ICP may exhibit varying outcomes in terms of ONSD.

## Conclusion

In summary, carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy increases ONSD. However, the change in ONSD values was significantly lower in the TIVA group than in the desflurane group, indicating that propofol-based anesthesia may mitigate ICP fluctuations during laparoscopic cholecystectomy. These results suggest that TIVA is a preferable anesthetic choice for patients undergoing surgery in the reverse Trendelenburg position.

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### Ethics

**Ethics Committee Approval:** University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital (approval number: 2019/514/148/19, date: 27/02/2019).

**Informed Consent:** All participants provided written informed consent.

### Authorship Contributions

Surgical and Medical Practices: S.S., E.H.Ü., M.K.B., M.A.Y., Concept: S.S., E.H.Ü., T.K., M.A.Y., Y.Y., K.T.S., Design: S.S., T.K., Y.Y., M.K.B., K.T.S., Data Collection or Processing: S.S., E.H.Ü., M.K.B., M.A.Y., Analysis or Interpretation: S.S., T.K., Y.Y., E.H.Ü., K.T.S., Literature Search: S.S., T.K., Y.Y., E.H.Ü., K.T.S., Writing: S.S., E.H.Ü., M.A.Y., K.T.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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