ORIGINAL ARTICLE

Cerebral Oximetry after Low Pressure *versus* Standard Pressure Pneumoperitoneum in Laparoscopic Nephrectomy

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ABSTRACT

Objective: To evaluate whether pneumoperitoneum pressure lower than the standard pressure would allow higher cerebral oxygen saturation (rSO_2) during laparoscopic nephrectomy (LN).
Study Design: Randomised controlled trial.
Place and Duration of Study: Ondokuz Mayis University Hospital, Samsun, Turkey, from January to November 2020.
Methodology: Sixty-two patients (aged 18-65 years; ASA I-III) scheduled for LN were equally divided into a low-pressure (LP; 8 mmHg) and standard-pressure (SP; 14 mmHg) group. Mechanical ventilator settings were adjusted to maintain 32-37 mmHg $ETCO_2$ and >96% SpO_2 throughout the surgery. The rSO_2 was evaluated by near-infrared spectroscopy before and one minute after induction and then every five minutes until patient transfer to the recovery unit. Oxygen and carbon dioxide partial pressures, pH, and haemoglobin, recorded at five minutes after induction, five and 30 minutes after insufflation, and 10 minutes after desufflation, were examined for correlations with rSO_2.
Results: Both groups had similar rSo_2, arterial blood gas, and haemoglobin values at all measurement times. The LP group showed no differences between the preoperative values and the values obtained at the different time points. In contrast, the SP group showed significant differences between the preoperative and the measured values (except at 25, 30, and 35 minutes) (p = 0.001). Four patients (12.9%) in both groups showed cerebral desaturation. The rSO_2 values were moderately correlated with the CO_2 and haemoglobin values.
Conclusion: Low insufflation pressure offered no advantages over standard pressure in terms of haemodynamics, arterial blood gases, cerebral oxygen saturation during LN, and CO_2 insufflation did not change rSO_2 levels.

Key Words: *Pneumoperitoneum, Spectroscopy, Oximetry, Nephrectomy, Surgery, Laparoscopic nephrectomy.*

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INTRODUCTION

Laparoscopy has become very popular in kidney surgery due to its association with better postoperative cardiorespiratory function, less postoperative pain, faster recovery, and early discharge.[1] Nevertheless, laparoscopic nephrectomy (LN) can cause significant changes in cerebral physiology, in addition to cardiovascular and respiratory changes, due to the patient's position and the long duration of pneumoperitoneum.[1,2]

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Decreases in respiratory system activity, lung compliance, volume, and capacity can lead to ventilation/perfusion mismatch and atelectasis.[2] Increase in intra-abdominal pressure and indirect increase in intrathoracic pressure can lead to cardiovascular effects, such as decreased preload, stroke volume, and cardiac output.[3] Increased intra-abdominal pressure and intrathoracic pressure also decreases cerebral venous drainage, increases intracranial pressure (ICP), and causes cerebral blood flow or volume changes. Hypercapnia occurring with carbon dioxide absorption during pneumoperitoneum can further increase ICP by causing vasodilation of cerebral vessels.[4,5]

Patients undergoing major urological surgery are often of an advanced age with multiple comorbidities. They are, therefore, at risk for complications related to pneumoperitoneum and positioning. These physiological changes may negatively affect cerebral oxygen saturation (rSO_2).[5] Lower than standard pressures may allow avoidance of these effects.

Herein, we test the hypothesis that higher rSO_2 levels can be attained with low pressure (LP, 8 mmHg) pneumoperitoneum compared to standard pressure (SP, 14 mmHg) in patients undergoing LN.

METHODOLOGY

This study was approved by the Clinical Research Ethics Committee (Approval No. B.30.2.ODM.0.20.08/1725) and registered at Clinical Trials.gov (NCT04671121, December 16, 2020).

All participants provided written informed consent before enrollment. This prospective, double-blind study included 62 American Society of Anaesthesiologists (ASA) Physical Status class I–III patients aged 18–65 years, who underwent LN (simple, partial, or radical).

Patients with cerebrovascular diseases (cerebral ischaemia or haemorrhage), neurological disorders (epilepsy, dementia, Parkinson's and Alzheimer's diseases) uncontrolled diabetes or hypertension, advanced organ failure (functional class III-IV heart failure or stages 3-5 chronic kidney disease), baseline peripheral oxygen saturation (SpO_2) less than 96%, or a haemoglobin <9 g dL-1 were excluded.

Patients were randomly assigned into two groups: Group LP received LP (n=31) and Group SP received SP pneumoperitoneum (n=31). Randomisation was performed using a computer-generated random number list, using the closed envelope method. Each patient was asked to choose an envelope, and the patients were assigned to the study, according to the group written in the envelope. Patients and anaesthesiologists were blinded to the group assignments. The CONSORT flow diagram is shown in Figure 1.

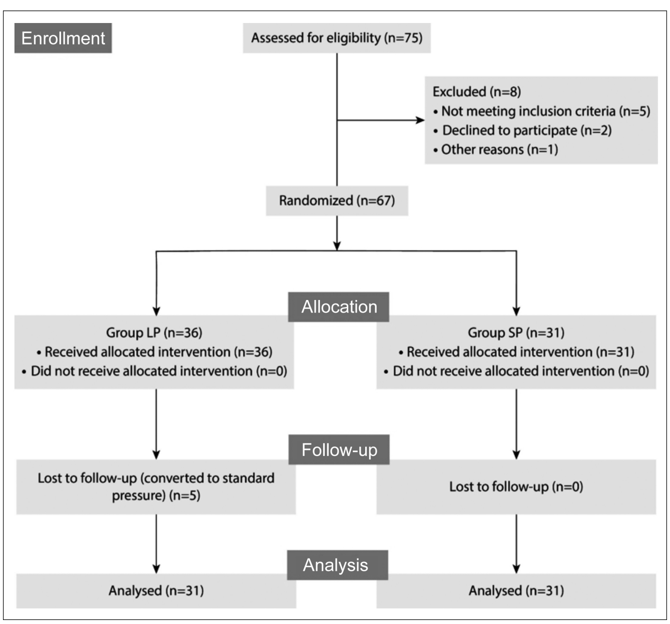

Figure 1: CONSORT flow diagram.

A standard anaesthesia protocol was used in both groups. Without premedication, patients were monitored with electrocardiogram, noninvasive blood pressure, peripheral oxygen saturation (SpO_2), rSO_2 (INVOS™ 5100C oximeter; Covidien, Mansfield, USA), and neuromuscular monitoring. Anaesthesia was induced with propofol, remifentanil, and rocuronium and maintained with O_2/Air, sevoflurane, and remifentanil IV infusion. A mechanical ventilator was used at standard settings. Pre-insufflation SpO_2 values were maintained at >96%, while respiratory rate was determined with end-tidal CO_2 ($EtCO_2$) of 32–37 mmHg.

CO_2 insufflation was performed in the patients who were placed in lateral semi-oblique (60°), and some flexion (jackknife) positions before the surgery were started. The mean arterial pressure (MAP), HR, SpO_2, and $ETCO_2$ were recorded at preoperative, at one minute after induction, and then every five minutes until the patient went to the recovery unit. MAP and HR values were kept at ± 20% of preoperative values by changing the remifentanil infusion rate. Hypotension and bradycardia were treated with noradrenaline 4–8 µg, atropine 0.5 mg. Patients who required noradrenaline or atropine more than twice were excluded.

For the rSO_2 measurements , before induction, the cerebral oximetry sensor was placed at least 2 cm above the eyebrows and 3 cm from the midline, in accordance with the manufacturer's instructions. Measurements were recorded at preoperative, at one minute after induction, and then every five minutes until the patient went to the recovery unit. Baseline values were accepted as the measurements obtained in the last 30 seconds of preoxygenation for three minutes with 80% oxygen before induction. Cerebral desaturation was defined as a decrease in the rSO_2 of >25% from the baseline value (if baseline value <50, reduction should be >20%), with this condition lasting ≥15 seconds. In this case, patient's normotension was first achieved, and the patient's neck was checked, and external factors that could cause arterial or venous obstruction, if any, were corrected. If no improvement was noted despite these efforts, the inspired oxygen concentration was removed 100%. The average of rSO_2 values from the right and left sensors at each measurement time were used to evaluate cerebral oxygenation.

Oxygen and carbon dioxide partial pressures (PaO_2 and $PaCO_2$), pH, and haemoglobin values were measured at the 5th minute (t1) after induction while the patient was in the supine position, at the 5th and 30th minutes after insufflation (t2, t3), while the patient was in the lateral semi-oblique position, and at 10 minutes after desufflation, while the patient was in the supine position (t4).

Baseline demographics, preoperative haemoglobin, duration of anaesthesia and surgery, lateral position time, pneumoperitoneum time, recovery time, procedure types, and pathological diagnosis were recorded. Recovery time was defined as time from discontinuation of sevoflurane and remifentanil to extubation at the end of the surgical procedure. Any complications that developed were also recorded.

Type I error and the strength of the study were 5% and 80%, respectively, with calculations performed with Minitab 16.0 software (Minitab Inc., State College, PA). The number of individuals for inclusion in each group was calculated as ≥28 to show a standard deviation of 7.4 and a difference of 5.72.[6] The sample size was increased by 10% to 31 patients per group to account for data losses. Data was analysed using SPSS (Version 22 for Windows, SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation, and frequency data were expressed as number and percentage (%). The Shapiro-Wilk test was used to evaluate the normal distribution of the data. Between--group comparisons were made with Student's t-test for normally distributed variables and the Mann-Whitney U-test for data without normal distribution. The Friedman test was used for within-group comparisons and the Spearman correlation test for changes in the rSO_2 values with time. The correlation coefficient (r) values were assessed as showing a 'weak' relationship if r = 0.00–0.24, 'moderate' if r = 0.25–0.49, 'strong' if r = 0.50–0.74 and 'very strong' if r = 0.75-1.00. A value of $p <0.05$ was considered statistically significant.

Table I: Demographics and operative times.

	Group LP (n=31) Mean±SD or Median (IQR)	Group SP (n=31) Mean±SD or Median (IQR)	*P-value*[*]
Age (year)	55.2±9.9	58.5±10.8	0.224
BMI (kg m^{-2})	27.1±5.1	29.6±4.2	0.139
Preoperative Hb (g dL^{-1})	13.4±2.0	13.8±2.0	0.462
ASA-PS Class	2 (1-2)	2 (2-2)	0.193[†]
Anaesthesia time (min)	123.3±29.0	137.4±42.6	0.156
Surgical time (min)	86 (75-102.5)	100 (90-129)	**0.040**[†‡]
Pneumoperitoneum time (min)	74.3±24.7	91.3±37.6	0.054
Lateral position time (min)	87.5 (73.7-100.0)	98 (77.5-130.0)	0.171[†]
Recovery time (min)	8 (10-11)	8.5 (7-11.5)	0.262[†]
Gender (Male/Female)	20 (64.5)/11 (35.5)	18 (58.1)/13 (41.9)	0.795
Comorbidities			
Cardiovascular system related[a]	14 (45.1)	15 (48.37)	
Endocrine system related[b]	6 (19.3)	6 (19.3)	0.729
Respiratory system related[c]	2 (6.4)	4 (12.9)	
None	9 (2.9)	6 (19.4)	
Nephrectomy			
Partial	17 (54.8)	15 (48.3)	0.966
Radical	12 (38.7)	14 (45.1)	
Simple	2 (6.4)	2 (6.4)	
ASA-PS class			
I	13 (41.9)	6 (19.4)	0.116
II	16 (51.6)	20 (64.5)	
III	2 (6.5)	5 (16.1)	<0.99
Pathologic diagnosis Malignant/Benign	28 (90.3)/3 (9.7)	28 (90.3)/3 (9.7)	

*Data are presented as mean ± standard deviation, median (IQR) or number (%). BMI: Body mass index; Hb: Haemoglobin concentration; ASA-PS: American Society of Anaesthesiologist Physical Status. [a]Hypertension, coronary artery disease; [b] Type 2 diabetes, goiter; [c]Asthma. *Student's t-test was used for the statistical analysis. [†]Mann-Whitney U-test was used for the statistical analysis. [†‡]p < 0.05 statistically significant versus group LP.*

RESULTS

Demographic data, anaesthesia, lateral position, pneumoperitoneum and recovery time were similar for all patients. Surgical durations were shorter in the LP group compared to SP group (median [IQR], 86 [75-102.5] and 100 [90-129], p = 0.040, respectively, Table I). The HR was higher in the LP group than in the SP group at 30 and 35 minutes (p = 0.019 and p = 0.018, respectively). The mean arterial pressure (MAP) was higher preoperatively in the LP group (p = 0.001) but higher in the SP group at 80 and 115 min (p = 0.019 and p = 0.012, respectively). The SpO_2 and $EtCO_2$ values were similar in both groups.

There was no marked difference in the rSO_2 (1423 measurements), arterial blood gas (ABG), and haemoglobin values in both groups at all measurement times (Figure 2, Table II). Within-group comparisons showed no differences between the preoperative values and other measurement times in the LP group (p = 0.939); however, significant differences were evident (except at 25, 30, and 35 minutes) in the SP group (p = 0.001). Cerebral desaturation occurred in four patients (12.9%) in both groups, but only during the insufflation period. All patients were treated by applying 100% oxygen.

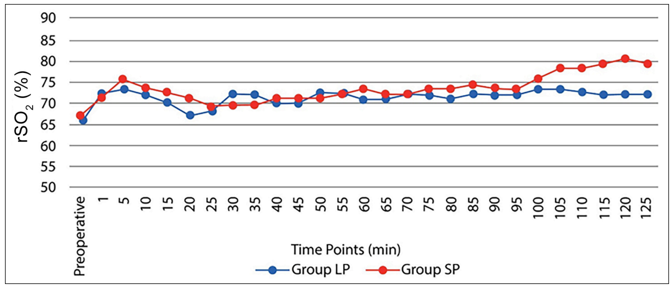

Figure 2: rSO_2 (%) values of the groups. rSO_2, regional cerebral oxygen saturation.

Table II: Arterial blood gas and haemoglobin values of the groups.

		Group LP (n=31) Mean ± SD	Group SP (n=31) Mean ± SD	*P-value*[*]
	pH	7.4±0.04	7.4±0.05	0.94
t_1	PaO_2 (mmHg)	288.7±91.3	305.0±78.3	0.47
	$PaCO_2$ (mmHg)	34.1±3.9	33.3±4.6	0.46
	Hb (g/dL)	12.2±1.7	12.3±2.1	0.84
	pH	7.4±0.05	7.3±0.05	0.30
t_2	PaO_2 (mmHg)	201.7±58.6	180.3±65.0	0.19
	$PaCO_2$ (mmHg)	35.2±5.3	35.8±4.1	0.64
	Hb (g/dL)	11.0±1.9	12.1±1.7	0.12
	pH		7.3±0.06	0.19
t_3	PaO_2 (mmHg)	194.6±76.4	168.2±54.7	0.17
	$PaCO_2$ (mmHg)	37.6±5.1	36.8±3.8	0.55
	Hb (g/dL)	10.7±2.0	11.6±2.6	0.38
t_4	pH	7.3±0.05	7.3±0.07	0.15
	PaO2 (mmHg)	199.2±79.7	179.7±63.8	0.37
	PaCO2 (mmHg)	37.3±3.8	39.4±5.5	0.14
	Hb (g/dL)	10.8±1.9	12.1±1.7	0.11

*Data are presented as mean ± standard deviation. PaO_2: Partial pressure of arterial oxygen; $PaCO_2$: Partial pressure of arterial carbon dioxide; Hb: Haemoglobin concentration. *Student's t-test was used for the statistical analysis. t_1: 5th minute post-induction with the patient in the supine position, t_2: 5th minute post-insufflation with the patient in the flank semi-oblique position, t_3: 30th minute post-insufflation with the patient in the flank semi-oblique position, t_4: 10th minute after desufflation with the patient in the supine position.*

A moderate positive correlation was detected between rSO_2 and CO_2 and haemoglobin in t1 (p = 0.001 and p = 0.002), a strong positive correlation between rSO_2 and haemoglobin in t2 (p=0.005), a moderate positive correlation between rSO_2 and CO_2 in t3 (p = 0.003), and a strong positive correlation between rSO_2 and CO_2 in t4 (p = 0.001). Only a moderate negative correlation was found with pH (p=0.024, Table III).

DISCUSSION

In this study, haemodynamics variables, ABG, haemoglobin and rSO_2 values of the LP and SP groups were similar. Following an increase in rSO_2 after induction in both groups, a slight downward trend was observed followed by constant course throughout. These changes were statistically significant in the SP group. Additionally, CO_2 and haemoglobin was found to have a moderate to strong positive correlation with rSO_2.

Table III: Relationship between rSO_2, arterial blood gas and haemoglobin values at t_1, t_2, t_3 and t_4.

rSO_2	t_1		t_2		t_3		t_4	
	r	*P-value*	r	*P-value*	r	*P-value*	r	*P-value*
pH	-0.137	0.314	-0.137	0.300	-0.124	0.397	-0.353	0.024*
PaO_2 (mmHg)	-0.179	0.187	0.052	0.694	-0.083	0.573	-0.167	0.298
$PaCO_2$ (mmHg)	0.446	0.001*	0.071	0.595	0.417	0.003*	0.507	0.001*
Hb (g dL^{-1})	0.487	0.002*	0.528	0.005*	0.176	0.399	0.438	0.053

*rSO_2: Regional cerebral oxygen saturation; r: Correlation coefficient; PaO_2: Partial pressure of arterial oxygen; $PaCO_2$: Partial pressure of arterial carbon dioxide; Hb: Haemoglobin concentration. *p <0.05 is statistically significant. t_1: 5th minute post-induction with the patient in the supine position, t_2: 5th minute post-insufflation with the patient in the flank semi-oblique position, t_3: 30th minute post-insufflation with the patient in the flank semi-oblique position, t_4: 10th minute after desufflation with the patient in the supine position.*

In the present study, cerebral oxygenation, hypoxia, physiological variables, and arterial blood gas values were similar in both groups. Previous studies evaluating the relationship between pneumoperitoneum and cerebral oxygenation have provided contradictory data: Inal *et al*. considered two different pneumoperitoneum pressures (10 *vs*. 14 mmHg) in laparoscopic cholecystectomy cases and reported higher rSO_2 values in the LP group;[6] whereas, LP did not affect the rSO_2 in this study. This may be due to greater frequency of rSO_2 data collection (5 *vs.* 15 minutes) and longer anaesthesia duration (~130 *vs.* 48 minutes) that allowed us to capture more changes in rSO_2. The reverse Trendelenburg position applied in cholecystectomy may also have exacerbated the cerebral effects of the pneumoperitoneum by reducing the cerebral blood volume.[7]

De Waal *et al.* showed increases in $ETCO_2$, cerebral blood volume, and rSO_2 after insufflation in children undergoing LP (5–8 mmHg) pneumoperitoneum during laparoscopic fundoplication,[8] as well as significant cerebral vasodilation with $PaCO_2$ and increased cerebral blood flow-volume. Conversely, the rSO_2 values in the LP group were similar to preoperative values. However, de Waal *et al*. determined baseline rSO_2 values after providing moderate hypocapnia and before insufflation and detected a ~25% increase in $PaCO_2$ throughout the pneumoperitoneum.

However, $ETCO_2$ and $PaCO_2$ values were similar in both our groups and may have prevented any rSO_2 changes caused by CO_2-induced cerebral vasodilation.

A comparison of laparoscopic (8–10 mmHg) and open pediatric appendectomy revealed no effect of pneumoperitoneum on rSO_2 values,[9] suggesting intact venous return and protection of cardiovascular stability when intraabdominal pressure <15 mmHg. Öztan *et al.* determined that pneumoperitoneum had no effect on haemodynamics, and their rSO_2 values were similar to those of the LP group.[10] Both these studies examined only ASA I patients, whereas 58.1% of our patients were ASA II–III; nevertheless, the rSO_2 values in these patients were similarly unaffected by pneumoperitoneum pressure.

Lee *et al.* reported a significant decrease in rSO_2 during laparoscopic (12–15 mmHg) gynecological surgery in a 15° Trendelenburg position and no increase due to pneumoperitoneum unless hypercapnia occurred.[11] The Trendelenburg position was proposed to increase ICP and decrease carotid artery blood flow, cerebral perfusion pressure, and rSO_2 values; whereas, pneumoperitoneum did not cause any change in cerebral blood flow and ICP as long as normocarbia was achieved. However, Park *et al*. found increased rSO_2 values in patients placed in the 30° Trendelenburg position during robotic surgery and associated this with the prevention of cerebral venous drainage by the Trendelenburg position, decreased venous drainage from the lumbar plexus with increased intraabdominal pressure with pneumoperitoneum, and increased cerebral blood volume and ICP due to increased $PaCO_2$.[12] Li *et al*. observed that rSO_2 increased with steep Trendelenburg position, and associated this with increased cerebral blood flow.[13] Conversely, Beck *et al*., in their study comparing robotic and open radical prostatectomy, found that steep Trendelenburg position and pneumoperitoneum did not impair cerebral autoregulation.[14]

In this study, where normocapnia was provided in all patients, it was found an increase in the SP group compared to the preoperative values. Park *et al.* suggested that a single mechanism seems unlikely to account for the increase of cerebral blood volume and ICP. Studies have shown a negative correlation between rSO_2 and ICP;[11,15] however, the increased cerebral oxyhaemoglobin with increased cerebral blood volume and reduction in haemoglobin and total haemoglobin may be responsible for increased rSO_2 values.[16] Moreover, the lateral position and slight flexion applied to these patients should not have affected cerebral haemodynamics to the extent of steep Trendelenburg position. The increase we detected in rSO_2 values was similar to that reported previously.[9,11]

Cerebral desaturation rates of ~8.5% have been reported in patients during different laparoscopic surgeries.[5,11] Cerebral desaturation was observed in more of our patients (~13%) than reported in previous studies. Tuna *et al*. found a much lower rate (5%); however, their data may reflect their inclusion of only ASA I patients; they also did not report the surgical position used.[9] Casati *et al.* found a cerebral desaturation rate of 20% in elderly abdominal surgery patients,[17] suggesting that older age (73 ± 5 years) and longer surgical duration (259 ± 94 minutes) could increase this rate.

One animal study reported positive correlation between intra-abdominal pressure and ICP.[18] In human patients with normal ICP, this increase has no detrimental effect, but it may worsen in patients with increased ICP (due to cerebral ischaemia, intracerebral lesion, or shunt).[19] However, increases in cerebral blood flow, which contributes to increases in ICP, is associated more with hypercapnia than with pneumoperitoneum and is absent under normocapnia.[20] The effects of pneumoperitoneum on cardiac output and cerebral oxygen saturation in children can also be minimised by optimising haemodynamic parameters.[21] In the present study, close haemodynamic monitoring and normocapnia prevented adverse effects of pneumoperitoneum pressure on cerebral oxygenation.

As mentioned earlier, pneumoperitoneum causes cardiorespiratory changes. However, literature shows that decreased lung compliance at standard *versus* LP does not affect $ETCO_2$, SpO_2, or arterial blood gases, in agreement with this study.[22-24] Cho *et al*. found no difference between static (HR and MAP) and dynamic cardiac parameters (cardiac and stroke volume index) in LP and SP groups undergoing laparoscopic colorectal surgery.[25] Similarly, a comparison of low and standard pressure in terms of cardiac functions reveals no difference between HR and MAP.[6]

This study has some limitations. Although most of our patients tolerated pneumoperitoneum without serious changes in rSO_2 values, cerebral desaturation occurred in some, and the potential effects of rSO_2 decreases on postoperative neurocognitive functions are unknown. The depth of anaesthesia may not have been constant, as volatile anaesthetic concentrations were not adjusted to the bispectral index value, so this may have affected rSO_2 values by disrupting the harmony between the cerebral blood flow and metabolic oxygen rate. ASA IV patients were also not included, where changes in rSO_2 could be more pronounced due to possible cardiorespiratory/cerebrovascular diseases.

CONCLUSION

There was no advantage of LP in terms of haemodynamic variables, arterial blood gases, and cerebral oxygen saturation. Most patients tolerate CO_2 insufflation without any significant rSO_2 changes; however, further studies should include patients with comorbid conditions affecting cerebral oxygenation and should evaluate postoperative cognitive functions.

ETHICAL APPROVAL:
The study was approved by the Institutional Ethics Committee of University of Ondokuz Mayis University. (Date: 16.12.2020, Approval No. B.30.2.ODM.0.20.08/1725).

PATIENTS' CONSENT:
Informed consents were obtained from all patients/relatives before the study began.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
CK, EK: Conceptualisation, methodology, software.
YBU, CK: Data curation, writing, original draft preparation.
BD, SB: Data curation, visualisation, investigation.
EO: Supervision.
BD, EK: Software, validation.
CK, BD, SB, YBU, EK, EO: Writing, reviewing and editing.

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