Article

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Impacts of Cerebral Oxygen Metabolism on Postoperative Nausea and Vomiting in Patients following Thyroid Surgery

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Background: Postoperative nausea and vomiting (PONV) is a common side effect after thyroidectomy, which can affect the recovery of patients who underwent thyroid surgery. It has been reported that cerebral oxygen metabolism may affect the occurrence of postoperative adverse reactions. Therefore, this study aimed to investigate the relationship between cerebral oxygen metabolism and PONV incidence in patients after thyroidectomy.
Methods: This study retrospectively analyzed the clinical data of 100 female patients who underwent thyroid surgery in a tertiary hospital between May 2022 and September 2023. The study participants were categorized into two groups: the Mannitol group (n = 50), patients who received an intravenous infusion of 0.5 g/kg mannitol at a rate of 150 drops/minute before the operation, and the Control group (n = 50), patients who intravenously received the equivalent volume of normal saline. All participants received the same anesthesia induction and maintenance treatment. During the surgery, we recorded their heart rate (HR), mean arterial pressure (MAP), urine volume, cerebral oxygen metabolism index (cerebral oxygen extraction ratio ($CERO_2$) and difference in arteriovenous oxygen (Da-jvO_2)) at each time point, including T0, 5 minutes after entering into the operating room; T1, 5 minutes after tracheal intubation; T2, immediately after cervical hyperextension; T3, immediately after the operation; T4, 50 minutes after the operation; T5, immediately at the operation stopped. Moreover, the incidence of PONV was assessed within 48 hours post-surgery.
Results: There were no statistical differences in HR and MAP between the two groups at each time point ($p > 0.05$). Compared to the Control group, urine output in the Mannitol group showed no significant changes at T0, T1, T2, and T3 ($p > 0.05$) but significantly increased at T4 and T5 time points ($p < 0.05$). Da-jvO_2 and $CERO_2$ in T1, T2, T3, T4 and T5 time points were significantly reduced compared to T0 ($p < 0.05$). Compared to T2 and T3, Da-jvO_2 and $CERO_2$ at T4 and T5 were significantly reduced in the Mannitol group ($p < 0.05$), but they showed no substantial changes in the Control group ($p > 0.05$). Furthermore, Da-jvO_2 and $CERO_2$ were significantly decreased at T4 and T5 time points in the Mannitol group compared to the Control group ($p < 0.05$). Additionally, PONV incidence was significantly lower (26.0%) in the Mannitol group compared to the Control group (50.0%) within 48 hours post-surgery ($p < 0.05$). The severity of PONV in the Control group was substantially higher than in the Mannitol group.
Conclusion: The preoperative intravenous infusion of mannitol can affect cerebral oxygen metabolism, thereby reducing the incidence and severity of PONV in patients who underwent thyroid surgery.

Keywords: postoperative nausea and vomiting; cerebral oxygen metabolism; thyroid surgery; mannitol

Introduction

Postoperative nausea and vomiting (PONV) is reported as one of the most prevalent side effects following general anesthesia, which is very complex due to various factors such as, anesthetic techniques, patient-related factors, and surgical elements [1]. The incidence of PONV varies widely, ranging from 20% in general surgery patients to as high as 80% in patients who underwent high-risk surgeries [2,3]. Thyroid surgery is reported as a common elective surgical procedure globally [4]. Following thyroidectomy, PONV is substantially common and significantly contributes to patient discomfort. Vigorous or recurrent vomiting poses challenges such as increased risk of postoperative bleeding, hematoma formation with subsequent obstruction of airway, incision pain, or dehiscence, potentially needing reparative surgery [5]. These factors can augment hospital stay, increase financial burden, and compromise the quality of postoperative recovery for patients [6]. Evidence indicates that PONV evokes greater fear among patients compared to postoperative pain, substantiating the significance of reducing PONV events following thyroid surgery [7].

Previous research has identified several known risk factors contributing to PONV incidence, including three primary aspects: anesthesia/medication-related factors (such as nitrous oxide, volatile agents, and opioids), patient-related factors (such as anxiety, gastrointestinal diseases, female gender, and metabolic diseases), and surgical factors (such as the nature of the procedure, duration of surgical procedure, and surgical technique) [8]. A previous study suggested that the Trendelenburg's position in laparoscopic surgery might affect blood flow resistance and intrathoracic pressure in the brain and further modulate cerebral oxygen saturation, thereby influencing the incidence of PONV post-laparoscopic surgery in female patients [9]. Moreover, different positions during shoulder arthroscopy have been found to affect regional cerebral tissue oxygen saturation levels, leading to cerebral desaturation events, which may influence the occurrence of nausea and vomiting [10]. These findings suggested that cerebral oxygen saturation might be a risk factor for PONV after surgery. Additionally, the cervical hyperextension position has been observed to potentially influence the blood flow velocity and flow of bilateral vertebral arteries compared to the horizontal position. Decreased average blood flow has been linked to adverse reactions, including vertigo and vomiting, in patients.

Regarding thyroidectomy procedures, it has been observed that the cervical hyperextension position during anesthesia administered for thyroidectomy could affect cerebral oxygenation and carotid blood flow [11]. Therefore, we hypothesized that the high PONV incidence in patients after thyroidectomy might be associated with cerebral oxygen metabolism. However, the precise relationship between cerebral oxygen metabolism and PONV incidence during thyroidectomy remains unclear.

This study aimed to explore whether cerebral oxygen metabolism in patients undergoing thyroidectomy could influence the incidence of PONV. In a previous study, mannitol, a diuretic, was utilized to reduce intracranial pressure, thereby regulating cerebral oxygen saturation during surgery [9]. Therefore, we used mannitol to reduce intracranial pressure before the operation. Furthermore, we investigated the correlation between cerebral oxygen metabolism and the occurrence of PONV in patients following thyroid surgery.

Materials and Methods

Population and Grouping

Female patients (n = 100) who underwent thyroid surgery at The First Hospital of Jiaxing, Affiliated to Jiaxing University between May 2022 and September 2023 were enrolled in this study. Each participant of the study provided written informed content.

The inclusion criteria were set as follows: (1) ASA grade I to II physical status (grade I: people have good development and nutrition, healthy physique, and normal function of each organ; grade II: besides surgical diseases, patients with sound function compensation have other mild diseases) [12]. (2) Patients aged between 20 and 65 years. (3) Body mass index (BMI) of the patients ranging from 18.5 to 24 kg/m^2. (4) Surgical procedures lasting over 60 minutes.

Moreover, exclusion criteria were as follows: (1) Recent use of anti-emetics within 48 hours before or after surgery. (2) Those with a history of smoking. (3) Patients with a history of PONV. (4) Those with a history of gastrointestinal disease. (5) Patients with severe cardiovascular and cerebrovascular diseases, liver and kidney function, and coagulation dysfunction. (6) Patients with preoperative hemoglobin level <90 g/L [13]. (7) Patients with contraindications to mannitol use.

The clinical data of the patients were retrospectively analyzed. Patients (n = 100) were divided into 2 groups: Mannitol group (n = 50), patients who underwent thyroidectomy and received an intravenous infusion of 0.5 g/kg mannitol (R004021; Kirsch Pharma, Salzgitter, Germany) at a rate of 150 drops/minute before the operation as previously described [9], and Control group (n = 50), patients who underwent thyroidectomy and received an equivalent amount of normal saline intravenously. All study participants in both groups were positioned in the cervical hyperextension position.

Written informed content was obtained from all participants, and this study received approval from the Ethics Committee of The First Hospital of Jiaxing, Affiliated to Jiaxing University (Approval number: 2022-KY-472). All procedures were conducted following the principles of the Declaration of Helsinki.

Anesthesia Induction and Maintenance

All patients received intravenous injections of sufentanil (H20054172, 0.6 µg/kg; Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China), midazolam (H20143222, 0.05 mg/kg; Nhwa, Xuzhou, China), propofol (H20123318, 1.5–2.0 mg/kg; Xi'an Libang Pharmaceutical Technology Co., Ltd., Xi'an, China), and vecuronium (H20084541, 0.2 mg/kg; Xi'an Libang Pharmaceutical Technology Co., Ltd., Xi'an, China). Laryngoscope-guided tracheal intubation was conducted and connected to an Anesthesia System Aesprie7900 anesthesia machine (Datex-Ohmeda Inc, Madison, WI, USA). PetCO2 levels were maintained at 35–45 mmHg range. Furthermore, patients were administered the intravenous injection of Lactated Ringer solution (H20033736 10 mL/kg·h; Anhui Double-Crane Pharmaceutical Co., Ltd., Wuhu, China). Moreover, remifentanil (H20030199, 0.15–0.20 µg/kg·min; Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China), propofol (H20123318, 6–8 mg/kg·h; Xi'an Libang Pharmaceutical Technology Co., Ltd., Xi'an, China), and intermittent vecuronium (H20084541, 2 mg/every 30 to 40 minutes; Xi'an Libang Pharmaceutical Technology Co., Ltd., Xi'an, China) were used for intraoperative anesthesia maintenance. Subsequently, patients were transferred to the PACU after surgery.

Observation Index

Tympanic temperature was immediately determined before anesthesia induction using a Thermoscan® infrared tympanic thermometer IRT4020 (Braun, Kronberg, Germany). The anesthesia duration, surgery time, and total volume of fluid infusion were analyzed for the two groups. The mean arterial pressure (MAP), urine volume, and heart rate (HR) were observed and recorded at various time points during each observation. The observation durations were as follows: T0, 5 minutes after entering the operating room; T1, 5 minutes after tracheal intubation; T2, immediately after cervical hyperextension; T3, immediately after the operation; T4, 50 minutes after the operation; T5, immediately at the operation ended.

The cerebral oxygen metabolism indices, including the cerebral oxygen extraction ratio ($CERO_2$) and the difference in arteriovenous oxygen (Da-jvO_2) were evaluated at each observation time point. Arterial and internal jugular vein bulb blood samples were collected. The levels of PaO_2, SaO_2, $PjvO_2$, and $SjvO_2$ were assessed using a blood gas analyzer (i-STATGA; Abbott Laboratories, Abbott Park, IL, USA) at each observation time point (T0, T1, T2, T3, T4, and T5). $CERO_2$ and Da-jvO_2 were calculated using the Fick formula as follows: $CaO_2 = 1.36 \times SaO_2 \times$ hemoglobin + $PaO_2 \times 0.0031$; $CjvO_2 = 1.36 \times SjvO_2 \times$ hemoglobin + $PjvO_2 \times 0.0031$; Da-$jvO_2 = CaO_2$–$CjvO_2$; $CERO_2 = (CaO_2–CjvO_2)/CaO_2 \times 100\%$.

Furthermore, we analyzed the occurrence rate of PONV within 48 hours after surgery. PONV events were classified based on the number of episodes, such as Grade I for no nausea and vomiting, Grade II for 1 to 2 episodes, Grade III for 3 to 4 episodes, and Grade IV for $\geq$5 episodes [14].

Statistical Analysis

Statistical analyses were conducted using SPSS 21.0 (SPSS Inc., Armonk, NY, USA). The data were expressed as the mean $\pm$ standard deviation. Comparison within groups was performed using repeated measures analysis of variance, and the independent sample *t*-test was applied for comparison between groups. The enumerated data were analyzed using the χ^2 test. A p value < 0.05 was regarded as statistically significant.

Results

We observed that there was no significant difference between the Mannitol group and the Control group regarding age, BMI, tympanic temperature, preoperative hemoglobin, anesthesia time, operation time, and fluid infusion volume ($p > 0.05$, Table 1).

There was no remarkable change in HR and MAP between the two groups at each time point ($p > 0.05$) (Table 2 and Figs. 1,2).

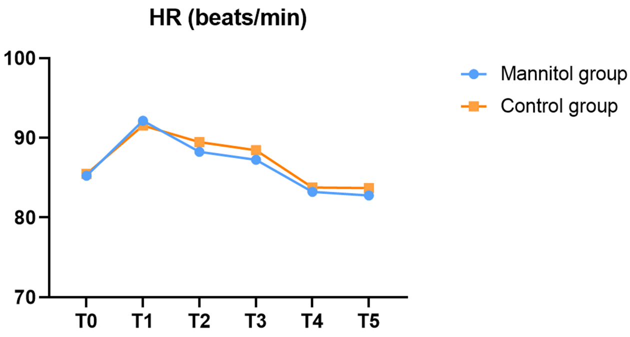

Fig. 1. Comparison of heart rate (HR) between the Mannitol and Control groups at each time point.

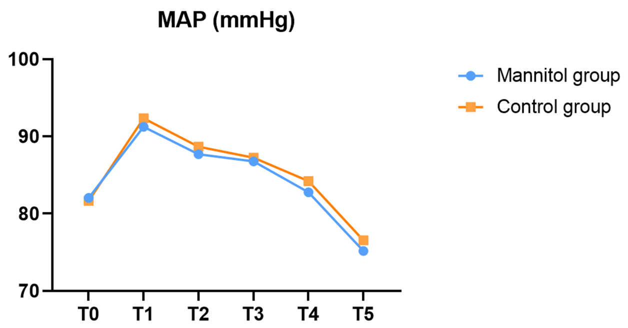

Fig. 2. Comparison of mean arterial pressure (MAP) between the Mannitol and Control groups at each time point.

Urine volume between the two groups at T0, T1, T2, and T3 time points did not show remarkable difference ($p > 0.05$, Table 3). However, at T4 and T5 time points, urine volume in the Mannitol group was substantially higher compared to the Control group ($p < 0.05$, Table 3, Fig. 3).

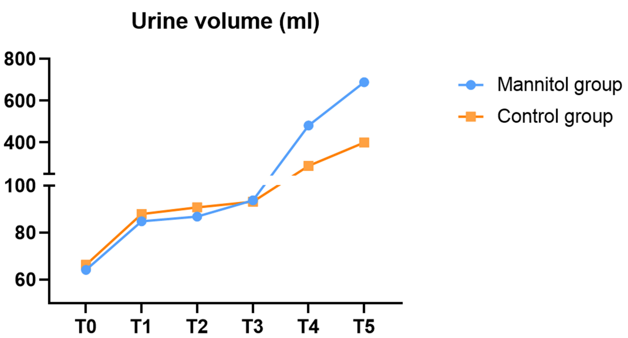

Fig. 3. Comparison of urine volume between the Mannitol and Control groups at each time point.

Table 1. Comparison of baseline information between the Mannitol and Control groups.

	Mannitol group (n = 50)	Control group (n = 50)	*t* value	*p* value
Age, years	45.38 ± 10.14	46.14 ± 9.66	0.384	0.702
BMI (kg/m^2)	21.34 ± 1.44	20.99 ± 1.59	1.154	0.251
Tympanic temperature (°C)	36.55 ± 0.13	36.61 ± 0.15	2.137	0.035
Preoperative hemoglobin (g/L)	125.63 ± 17.25	127.69 ± 16.38	0.612	0.542
Anesthesia time (min)	112.37 ± 11.46	115.13 ± 11.14	1.221	0.225
Operation time (min)	91.03 ± 11.12	91.46 ± 11.36	0.191	0.849
Fluid infusion volume (mL)	967.42 ± 187.24	944.13 ± 177.68	0.638	0.525

BMI, Body mass index.

Table 2. Comparison of HR and MAP between the Mannitol and Control groups at each time point.

Group	T0	T1	T2	T3	T4	T5
HR (beats/min)						
Mannitol group (n = 50)	85.23 ± 12.24	92.13 ± 12.56	88.24 ± 12.53	87.24 ± 11.78	83.21 ± 11.75	82.76 ± 11.58
Control group (n = 50)	85.46 ± 11.54	91.55 ± 12.77	89.46 ± 12.89	88.43 ± 11.24	83.76 ± 11.22	83.69 ± 12.23
t value	0.097	0.229	0.480	0.517	0.239	0.390
p value	0.923	0.819	0.632	0.606	0.811	0.697
MAP (mmHg)						
Mannitol group (n = 50)	82.03 ± 9.98	91.23 ± 12.55	87.68 ± 12.88	86.77 ± 15.67	82.76 ± 9.88	75.16 ± 9.76
Control group (n = 50)	81.66 ± 10.36	92.34 ± 12.96	88.66 ± 13.26	87.24 ± 14.79	84.22 ± 10.48	76.55 ± 10.03
t value	0.182	0.435	0.375	0.154	0.717	0.702
p value	0.856	0.664	0.709	0.878	0.475	0.484

Note: HR, heart rate; MAP, mean arterial pressure; T0, 5 minutes after passing into the operating room; T1, 5 minutes after tracheal intubation; T2, immediately after cervical hyperextension; T3, immediately after surgery; T4, 50 minutes after surgery; T5, immediately at the operation stopped.

Table 3. Comparison of urine volume (mL) between the Mannitol and Control groups at each time point.

Group	T0 (mL)	T1 (mL)	T2 (mL)	T3 (mL)	T4 (mL)	T5 (mL)
Mannitol group (n = 50)	64.11 ± 11.54	84.79 ± 9.93	86.77 ± 9.88	93.68 ± 12.77	481.24 ± 62.13*	688.47 ± 58.67*
Control group (n = 50)	66.33 ± 12.68	87.86 ± 11.45	90.74 ± 11.33	93.12 ± 10.88	288.41 ± 49.68	399.56 ± 54.77
t value	0.916	1.432	1.867	0.236	17.140	25.453
p value	0.362	0.155	0.065	0.814	0.000	0.000

*$p < 0.05$ vs. Control group at each time point.

Compared with T0 time point, Da-jvO_2 and CERO_2 in T1, T2, T3, T4 and T5 time points were significantly decreased ($p < 0.05$). Compared with T2 and T3, Da-jvO_2 and CERO_2 at T4 and T5 were remarkably decreased in the Mannitol group ($p < 0.05$), but both showed no obvious changes in the Control group ($p > 0.05$). Da-jvO_2 and CERO_2 were significantly decreased at T4 and T5 time points in the Mannitol group relative to the Control group ($p < 0.05$) (Table 4).

The occurrence rate of PONV in the Mannitol group (26.0%) was significantly lower compared to the Control group (50.0%) within 48 hours post-surgery ($p < 0.05$). Moreover, the severity of PONV was substantially higher in the Control group than in the Mannitol group (Table 5).

Discussion

Considering the good malignancy prognosis and low mortality associated with thyroid cancer, the post-surgery quality of life for patients is as important as the control of the disease [15]. Reducing the incidence of postoperative complications and promoting rapid rehabilitation of patients have gained attention in thyroidectomy [16,17]. PONV is a common unfavorable postoperative complication post thyroid surgery, which has been recognized as a leading cause of discomfort during postoperative thyroidectomy recovery [18]. Nevertheless, the exact etiologies of PONV post-thyroidectomy remain unclear. Several factors, such as sex, age, anesthetic technique, menstruation, obesity, and preoperative vagal stimulation have been demonstrated to contribute to PONV occurrence [19–21]. Moreover, accumulating evidence indicates a correlation between cerebral tissue oxygen saturation and the fre-

Table 4. Comparison of cerebral oxygen metabolism indexes between Mannitol and Control groups at each time point.

Group	T0	T1	T2	T3	T4	T5
$Da\text{-}jvO_2$ (mL/L)						
Mannitol group (n = 50)	57.33 ± 6.35	46.57 ± 6.19 [a]	44.64 ± 6.16 [a]	43.35 ± 5.59 [a]	36.54 ± 5.85 [ab*]	37.47 ± 6.16 [ab*]
Control group (n = 50)	58.42 ± 7.36	47.78 ± 6.49 [a]	45.44 ± 5.99 [a]	44.87 ± 6.15 [a]	46.95 ± 5.68 [a]	47.66 ± 6.11 [a]
$CERO_2$ (%)						
Mannitol group (n = 50)	39.12 ± 5.62	32.68 ± 4.52 [a]	30.89 ± 4.43 [a]	29.64 ± 4.26 [a]	23.88 ± 4.32 [ab*]	24.24 ± 4.96 [ab*]
Control group (n = 50)	39.34 ± 5.14	33.38 ± 4.84 [a]	31.41 ± 4.79 [a]	31.02 ± 5.12 [a]	31.78 ± 5.56 [a]	32.77 ± 4.88 [a]

Note: Intra-group comparison with T0, $^{a}p < 0.05$; Intra-group comparison with T2 or T3, $^{b}p < 0.05$. At the same time point, the Mannitol group was compared with the Control group, $^{*}p < 0.05$. $CERO_2$, cerebral oxygen extraction ratio; $Da\text{-}jvO_2$, difference in arteriovenous oxygen.

Table 5. Comparison of PONV occurrence rate between the Mannitol and Control groups.

Group	PONV grade				PONV incidence
	I	II	III	IV	
Mannitol group (n = 50)	37 (74.0%)	4 (8.0%)	4 (8.0%)	5 (10.0%)	13 (26.0%)
Control group (n = 50)	25 (50.0%)	9 (18.0%)	8 (16.0%)	8 (16.0%)	25 (50.0%)
χ^2 value					6.112
p value					0.013

Note: PONV, postoperative nausea and vomiting.

quency of PONV after surgery [9,10,22]. However, the correlation between cerebral oxygen metabolism and PONV occurrence after thyroidectomy in patients remains ambiguous.

It has been reported that mannitol could decrease blood viscosity, increase cerebral blood flow, alleviate intracranial pressure, and improve microcirculation and cerebral oxygenation [23,24]. The use of mannitol during retroperitoneal laparoscopic surgery has been shown to elevate the cerebral oxygen content in patients, and preoperative use of mannitol (0.5 mg/kg) has been found safe and effective in alleviating side effects, like renal failure, hypotension and electrolyte disturbances [25,26]. Moreover, mannitol has been indicated to decrease intracranial pressure by increasing urine output and brain blood flow, thereby ameliorating the release of inflammatory mediators, affecting cerebral tissue oxygen saturation, and potentially preventing PONV occurrence after gynecological laparoscopic surgery [9]. Thus, our study used mannitol treatment in patients undergoing thyroidectomy to explore its impact on cerebral oxygen metabolism and PONV incidence. In this study, urine volume was utilized for reflecting changes in intracranial pressure, and our data indicated that mannitol treatment markedly increased the postoperative urine volume at T4 and T5 time points relative to the Control group, suggesting that mannitol could decrease the intracranial pressure. A previous study reported that mannitol could affect cerebral oxygen saturation in female patients who underwent laparoscopy surgery, thereby influencing the incidence of postoperative PONV [9].

Oxygen supply and consumption in the brain tissues are regarded as normal aerobic metabolism vital indicators. Monitoring the balance between cerebral oxygen supply and demand may be crucial for protecting the brain during surgical anesthesia [27]. $Da\text{-}jvO_2$ and $CERO_2$ are the key indices of cerebral oxygen metabolism [28,29]. Our findings revealed a substantial decrease in both $Da\text{-}jvO_2$ and $CERO_2$ values after anesthesia, suggesting that the combination of sufentanil, midazolam, and propofol could reduce the rate of cerebral oxygen uptake. Moreover, at T4 and T5 time points, $Da\text{-}jvO_2$ and $CERO_2$ values in the Mannitol group were significantly elevated relative to the Control group. This impact may be attributed to the intracranial pressure-reducing effect, which might reduce cerebral oxygen metabolism.

In the current study, the occurrence rate of PONV within 48 hours post thyroidectomy was significantly decreased in the Mannitol group relative to the Control group (26.0% vs 50.0%). Furthermore, mannitol treatment was found to reduce cerebral oxygen metabolism in patients undergoing thyroidectomy. These findings indicate a potential association between cerebral oxygen metabolism and PONV incidence in patients after thyroidectomy. However, there were some limitations in the current study, including a small sample size and an unclear mechanism underlying the impact of cerebral oxygen metabolism on PONV incidence.

Conclusion

The preoperative use of mannitol decreased both $CERO_2$ and $Da\text{-}jvO_2$, effectively affecting cerebral oxygen metabolism, which contributed to a lower incidence of PONV after thyroidectomy in patients. This finding might offer valuable insights into preventing PONV in patients after thyroidectomy.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

QQ, CYW and XS designed the research study. QQ and CYW performed the research. QQ analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Written informed content was obtained from all participants, and this study received approval from the Ethics Committee of The First Hospital of Jiaxing, Affiliated to Jiaxing University (Approval number: 2022-KY-472). All procedures were conducted following the principles of the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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