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Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G Corresponding Author: Source of support Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Background: Back		ABCDEF AEG AG BE BC EF A AB	Lixia Li Lei Zhao Tianlong Wang Na Xu Ping Wang Yi An Zhongjia Li Liqun Jiao Bin Yang	Department of Anesthesiology, Xuanwu Hospital, Capital Medical University, Beijing, P.R. China	
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		kground: Aethods:	This study aimed to determine the effects of alveolar recruitment maneuver (RM) on cerebral oxygen satura- tion and cerebral blood velocity in patients undergoing carotid endarterectomy (CEA) before clamping of the carotid artery. In this crossover exploratory study, all patients were randomized to undergo an RM (30 cmH ₂ O of continuous airway pressure for 30 s) and a "sham" maneuver (SM; 5 cmH ₂ O for 30 s), followed by an alternative interven- tion after a 5-min equilibration period. Near-infrared spectroscopy (NIRS) was used to monitor regional cere- bral oxygen saturation (rSO ₂), and transcranial Doppler ultrasonography (TCD) to evaluate blood velocity of the middle cerebral artery (V-MCA). Changes in rSO ₂ , V-MCA, mean arterial pressure (MAP), and heart rate (HR) in response to the 2 interventions were compared. A total of 59 patients underwent the study procedure. RM reduced rSO ₂ , V-MCA, MAP, and HR, but these vari- ables slightly changed during SM. A significant drop in rSO ₂ was observed immediately after RM compared with the baseline value (68.51±4.4% vs 64.12±5.15%; P<0.001). The decrease in rSO ₂ was higher during the RM than during the SM (-6±4% vs 1±2%; P<0.001). Similarly, change in V-MCA was more significant in response to RM than SM (-26±19% vs 19±16%; P<0.001). The V-MCA value changed from 39 cm/s to 29 cm/s after RM. In addition, V-MCA of the ipsilateral to the surgical side decreased more obviously than the contralateral side (-26±19% vs -20±17%; P=0.001). An RM at 30 cmH ₂ O of continuous airway pressure for 30 s decreased rSO ₂ and V-MCA. In addition, MAP and HR were affected. Anoxia • Endarterectomy, Carotid • Hypoxia-Ischemia, Brain		
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Background

Carotid endarterectomy (CEA) is effective in preventing stroke for both symptomatic and asymptomatic carotid stenosis [1,2]. However, clamping of the carotid artery during CEA may lead to cerebral ischemia and brain damage [3,4]. Furthermore, the procedure may lead to airway edema owing to the proximity of the surgery to the trachea. Postoperative bleeding results in neck hematoma, airway compression, and other injuries, further increasing the incidence of postoperative respiratory complications and prolonging the time of postoperative recovery [5,6]. Approximately 75% of CEA surgeries are performed under general anesthesia with endotracheal intubation [7]. However, because of the development of atelectasis, mechanical ventilation may impair oxygenation [8-10]. A strategy of protective ventilation using a recruitment maneuver (RM) of 30 cmH₂O of continuous airway pressure for 30 s in addition to small tidal volumes and a high positive end-expiratory pressure is reported to limit atelectasis [11]. Thus, RM may improve clinical outcome in this population.

Owing to its clinical benefits of increasing oxygenation and reducing postoperative complications, the strategy of protective ventilation contained with RM has gained widespread acceptance [11-13]. In recent years, RM has been advocated to treat not only patients with a severe respiratory disease requiring mechanical ventilation, such as patients with acute respiratory distress syndrome (ARDS), but also patients with normal lung function undergoing general anesthesia in the operating room and to safely and effectively improve lung compliance and perioperative oxygenation [11,12,14]. However, some studies have reported that RM is associated with transient hemodynamic fluctuations [15]. Previous studies on neurosurgical patients undergoing supratentorial tumor resection have reported increased subdural pressure and reduced the cerebral perfusion pressure (CPP) during an RM [16]. An RM of 30 cmH₂O of continuous airway pressure for 30 s can re-expand the atelectatic lung tissue to reduce the incidence of postoperative respiratory complications; however, the effect of high airway pressures on the cerebral perfusion in patients with carotid artery stenosis is unknown [13,14]. Hence, this study aimed to explore whether an intraoperative RM had an effect on the cerebral perfusion.

For efficacy and safety in detecting cerebral ischemia during CEA, the most widely used intraoperative monitoring strategies to guide the shunt placement appropriately are transcranial Doppler ultrasonography (TCD) and near-infrared spectroscopy (NIRS) [17-19]. The application of TCD monitoring can reduce shunt and the incidence of shunt-related complications [19]. Optimization of regional cerebral oxygen saturation (rSO₂) can improve postoperative outcomes, and low cerebral oxygen saturation seems to be associated with postoperative adverse

events [18]. TCD can continuously monitor changes in the velocity of the middle cerebral artery (V-MCA) and may indicate changes in intracranial perfusion [1,19,20]. NIRS can monitor the balance of cerebral oxygen supply and demand [21,22]. This study aimed to determine the effect of an intraoperative RM on rSO₂ by NIRS in patients with carotid artery stenosis undergoing CEA and to observe the change of V-MCA by TCD and hemodynamics changes during the study.

Material and Methods

This prospective crossover exploratory study was conducted from March 2018 to December 2018 at the Xuanwu Hospital, Beijing, China. This study was approved by the Clinical Research Ethics Board of the University of Xuanwu Hospital of Capital Medical University in March 2018. The trial was registered with China Clinical Trial Registry (registration number, ChiCTR1800014564; principal investigator, Lei Zhao; date of registration, January 21, 2018). A total of 70 patients scheduled for CEA were included and provided written informed consent before participation.

Intervention

In this crossover exploratory study, all patients were randomized to undergo an RM (30 cmH₂O of continuous airway pressure for 30 s) and a "sham" maneuver (SM; 5 cmH₂O for 30 s), followed by an alternative intervention after a 5-min equilibration period (**Figure 1**). During the intervention, the patient had no spontaneous breathing. After each maneuver, the ventilation parameters were maintained as before. The surgical procedure was suspended during intervention. After the second maneuver and measurements, all measurement were obtained and the study was terminated and the surgery proceeded as planned.

We set an SM for exploring the effect of an intraoperative RM on rSO₂ and V-MCA to eliminate the possible effect of simple apnea on rSO₂ and V-MCA during RM. The study was conducted after muscle relaxation and endotracheal intubation, but before clamping of the internal carotid artery (ICA). The study was initiated 10-20 min after the induction of anesthesia and fluid administration to obtain hemodynamic stabilization.

The maneuver was terminated if rSO_2 decreased by >20% and/ or V-MCA by >50% for >2 min. In case of such reductions in rSO_2 or V-MCA, the intervention (RM or sham RM) was terminated and appropriate measures were taken, such as improving inhaled oxygen concentration or elevating blood pressure to improve cerebral blood flow, because it was presumed that severe intracranial ischemia might occur, which patients might not be able to tolerate [23,24].



Figure 1. Randomized crossover study design involved 2 intervention periods: a recruitment maneuver (RM) of 30 cmH_2O for 30 s and a sham maneuver (SM) of 5 cmH_2O for 30 s at a different time point; the 2 procedures were separated by an equilibration period of 5 minutes. The observation targets were measured before and after each intervention period (pre-post RM and SM).

Study Population

Patients age >40 years, with American Society of Anesthesiologists class II-III, and scheduled for CEA were eligible to participate in the study. Patients accepted the surgery for carotid stenosis caused by different degrees of atherosclerotic plaque formation in the carotid artery. Patients with severe hypertension (>180/110 mmHg), recent cerebral infarction (<4 weeks), or hemorrhagic stroke and pregnant and lactating women were excluded. Patients with severe heart disease (eg, left ventricular ejection fraction of <40%, myocardial infarction for <6 months, significant valvular disease), severe pulmonary disease that needs long-term oxygen therapy, asthma, pulmonary bullae, a history of pneumothorax, or previous lung resection, who could not tolerate RM, were also excluded.

Anesthetic Management

All participants were monitored according to routine clinical practice, such as electrocardiogram, noninvasive blood pressure, continuous intraarterial blood pressure (via the radial artery), continuous pulse oximetry monitoring, bispectral index (BIS), and end-tidal carbon dioxide ($P_{\rm ET}CO_2$). In addition, the patients were continuously monitored using NIRS and TCD throughout the surgery. The rSO₂ was monitored using NIRS (CAS Medical Systems, Inc, Branford, CT) with optodes placed bilaterally on the forehead. The bilateral V-MCA was monitored using TCD (The Elica Company, Shenzhen, China), using a probe with a specially designed headband fixed to the patient's head [25].

To prevent hypotension after induction, all patients were given 6 mL/kg fluid volume for supplementary dilatation. Anesthesia was induced and maintained according to clinical practice by the same attending anesthesiologist. After adequate preoxygenation with 100% oxygen, anesthesia was induced by sufentanil 0.3 μ g/kg, etomidate 0.2 mg/kg, and rocuronium 0.6 mg/kg. After effective muscle relaxation, tracheal intubation assisted with the GlideScope video laryngoscope was performed. The ventilation model was pressure-controlled ventilation with a volume guarantee, tidal volume was 6 mL/kg, fraction of inspired oxygen was 50%, inspiration-to-expiration ratio was 1: 2, SpO_2 was maintained at 98%, and $P_{ET}CO_2$ was monitored and maintained between 35 and 45 mmHg [26].

Anesthesia was maintained with total intravenous anesthesia using propofol and remifentanil. The initial concentration of propofol was 3 mg/(kg/h), and the adjustment range was set at 0.5 mg/(kg/h) to maintain BIS between 40 and 60. Remifentanil for continuous intravenous analgesia was maintained at 0.1-0.4 μ g/(kg/min) according to surgical stimulation. Intraoperative SpO₂ was maintained at 98-100%, and the body temperature was maintained at 36-37°C.

Data Collection

Baseline characteristics were obtained from the participants' medical records. To obtain the partial pressure of arterial blood carbon dioxide (PaCO₂), after the induction of anesthesia, arterial blood was sampled for gas analysis before intervention of lung recruitment. The difference between PaCO₂ and P_{ET}CO₂ was determined and used to estimate PaCO₂ from P_{ET}CO₂ at the following time points.

Data on V-MCA, rSO_2 , and hemodynamics were collected over 30 s before and after both RM (pre-RM and post-RM) and sham RM (pre-SM and post-SM). To account for differences between individuals, data changes were expressed as the rise or fall of the percentage, calculated using the following formula: post-pre/pre×100%.

Statistical Analysis

Continuous variables were presented as mean±standard deviation and categorical variables as number (percentages). The Shapiro–Wilk test was used to evaluate data normality. Using the paired *t* test or Wilcoxon test of 2 related samples for normally distributed and skewed data, respectively, changes in rSO₂, V-MCA, HR, and mean arterial pressure (MAP) were compared (pre-RM vs post-RM ad pre-SM vs post-SM), changes in response to RM and SM were evaluated, and ipsi- and



Figure 2. Flow diagram. RM – recruitment maneuver; SM – sham recruitment maneuver; rSO₂ – regional oxygen saturation; V-MCA – blood flow velocity of the middle cerebral artery; HR – heart rate; MAP – mean arterial pressure.

contralateral changes in rSO2 and V-MCA were compared. In addition, the Spearman's rank correlation coefficient was used to examine whether the changes in heart rate (HR) and MAP were consistent with the changes in rSO₂ and V-MCA and the correlation in the changes of rSO₂ and V-MCA. To evaluate whether there was any carryover, the Mann-Whitney *U* test or the 2 independent samples *t* test was used to compare changes in rSO₂ and V-MCA in response to RM for patients in the RM first and SM first groups. SPSS version 21.0 was used for all statistical analyses. *P*<0.05 was considered statistically significant.

Results

A total of 80 patients were assessed for eligibility, 10 of whom were excluded before the surgery because they did not meet the inclusion criteria (n=4), TCD did not have an adequate temporal window (n=3), and they refused to participate (n=3). Furthermore, 11 patients were excluded after randomization because of incomplete intraoperative data recording. Thus, 59 patients completed the study (**Figure 2**).

The characteristics of the study participants are presented in **Table 1**. The baseline rSO_2 , V-MCA, MAP, and HR in the 2 maneuvers (RM and SM) are presented in **Table 2**. There were no significant differences in the baseline information (pre-RM vs pre-SM; *P*>0.05). Without taking any additional measures, all variables had returned to the baseline value in both groups after the 5-min equilibrium between evaluations.

The effect of the RM and SM is presented in **Table 2**. There were no significant differences in the baseline information (pre-RM vs pre-SM; P>0.05). The rSO₂ value of ipsilateral to

 Table 1. Characteristics of the study population.

Variable	Overal	l (n=59)	
Age	6	2±8	
Body mass index	25±3		
ASA			
II	16	(26%)	
III	43	(73%)	
Cerebral infarction	48	(81%)	
Hypertension	39	(66%)	
Diabetes mellitus	18	(31%)	
Coronary heart disease	11	(19%)	
Severe stenosis of contralateral ICA	9	(15%)	
Collateral circulation	43	(73%)	
Recruitment maneuver first	32	(54%)	

Data are expressed as number (percentage) or mean±standard deviation for n=59. Hypertension is defined as systolic blood pressure between 140 mmHg and 180 mmHg and diastolic blood pressure between 90 mmHg and 110 mmHg. Severe stenosis of contralateral ICA is defined as stenosis of contralateral ICA greater than 70% diagnosed by preoperative digital subtraction angiography. Collateral circulation is defined as anterior or posterior branches open detected by preoperative transcranial color-coded duplex. ASA – American Society of Anesthesiologists; ICA – internal carotid artery.

the surgical side had a significant drop immediately after the RM (69±4% vs 64±5%; P<0.001). Changes in rSO₂ during SM was insignificant. RM reduced V-MCA from 39 ± 11 cm/s to 29 ± 12 cm/s (P<0.001). However, during the SM maneuver,

Variable	Pre-RM	Post-RM	Pre-SM	Post-SM
HR (beat/min)	54 <u>+</u> 8	53±8*	56±8	56±8
MAP (mmHg)	97 <u>+</u> 9	71±14*	97±9	100±9
IrSO ₂ (%)	69±4	64±5*	68±4	69 <u>±</u> 4
CrSO ₂ (%)	68±5	65±5*	68±5	69 <u>±</u> 4
IV-MCA (cm/s)	39±11	29±12*	39±11	45±14**
CV-MCA (cm/s)	47 <u>±</u> 15	38±15*	47±15	57±19**
PaCO ₂ (mmHg)	38±4	31±8*	37±4	40±6**

 Table 2. Comparison of pre- and post-RM and pre- and post-SM.

* P<0.05, compared with pre-RM; ** P<0.05, compared with pre-SM. $CrSO_2$ – the rSO_2 value of the contralateral side; CV-MCA – the V-MCA value of the contralateral side; HR – heart rate; $IrSO_2$ – the rSO_2 value of the surgical side (ipsilateral rSO_2); IV-MCA – the V-MCA value of the surgical side (ipsilateral V-MCA); MAP – mean arterial pressure; $PaCO_2$ – arterial partial pressure of carbon dioxide; RM – recruitment maneuver; SM – sham maneuver.

the V-MCA value was 45 ± 14 cm/s after SM, which was higher than the value before (39 ± 11 cm/s; P<0.001). The value of PaCO₂ was higher after SM (40 ± 6 mmHg) than after RM (31 ± 8 mmHg; P<0.001). In addition, the changes in the MAP reduced significantly at RM maneuver.

Changes in the rSO₂ (*P*=0.276) and V-MCA (*P*=0.584) during RM were similar between patients who underwent the RM first and those who underwent the SM first. The comparisons of relative changes between the 2 treatment periods are shown in **Figure 3**. Both rSO₂ and V-MCA dropped significantly in RM compared with those in SM. The relative change in the rSO₂ between RM and SM was -6±4% vs 1±2% (*P*<0.001). The relative change in the V-MCA between RM and SM was -26±19% vs 19±16% (*P*<0.001). In addition, during RM maneuver, relative changes of V-MCA are more significant in the ipsilateral side (-26±19%; *P*=0.001) than the contralateral side (-20±17%). Changes in ipsi- and contralateral rSO₂ were similar. Relative changes in HR and MAP were also affected. During RM, the HR changed slightly compared with SM. MAP had a more significant decrease during the RM than SM.

The correlation analysis revealed that the changes in MAP were correlated with the changes in rSO_2 (r, 0.720; P<0.001) and V-MCA during RM (r, 0.557; P<0.001). Moreover, the changes in rSO_2 during RM were correlated with the changes in V-MCA (r, 566; P<0.001). In addition, the changes in PaCO₂ also correlated with the changes in V-MCA (r, 0.275; P=0.037) (**Table 3**). During SM maneuver, the changes in the variables were not correlated with the changes in rSO_2 and V-MCA (P>0.05).

Discussion

This study used an intraoperative neuromonitoring technology to explore the effects of RM on the cerebral oxygen saturation and cerebral blood velocity of patients undergoing CEA. The results indicated that RM reduced cerebral oxygen saturation by NIRS and cerebral blood velocity by TCD. This study found that during RM, the rSO₂ and V-MCA relatively decreased by 6% and 26% from baseline values, respectively. Several studies considered the relative value of rSO₂ and V-MCA that decreased by 20% and 50%, respectively, as a cutoff value, which indicates insufficient cerebral perfusion which may cause severe cerebral ischemia during CEA [19,27,28]. The reduction in rSO₂ and V-MCA did not reach the threshold of severe cerebral ischemia in our study. However, changes in rSO₂, and V-MCA also indicated that RM may affect cerebral perfusion in patients with carotid artery stenosis.

Intraoperative NIRS monitoring is increasingly used routinely in various surgery. Several studies have examined the relationship between intraoperative rSO₂ and postoperative neurological complications, particularly neurocognitive outcomes. Desaturation of rSO, increased the risk of postoperative cognitive dysfunction, and was associated with postoperative delirium and prolonged intensive care unit (ICU) and hospital stay [29,30]. Colak's [31] study proved that intraoperative rSO, monitoring and measures to correct cerebral oxygen desaturation in a timely manner have resulted in a better cognitive outcome of patients who underwent coronary artery bypass grafting. Deschamps et al [18] established a physiologic algorithmic approach to the reversal of decreases in cerebral oxygen saturation, and it was feasible. They showed that rSO₂-oriented perioperative management can avoid further progression of cerebral oxygen desaturations and reduce the incidence of postoperative complications. Moreover, a systematic review [32]



Figure 3. Relative changes in regional cerebral oxygenation (rSO₂) and middle cerebral artery blood velocity (V-MCA) ipsilateral to the surgical side, mean arterial pressure (MAP), and heart rate (HR) from baseline in response to a recruitment maneuver (RM) and sham maneuver (SM), respectively. Changes in ipsilateral side (I) and contralateral side (C) were also compared. Values are mean±SD. (A) Changes of rSO₂ comparison; # P<0.05, RM-IrSO₂ vs SM-IrSO₂; ## P<0.05, RM-CrSO₂ vs SM-CrSO₂; (B) Changes of V-MCA comparison; # P<0.05, RM IV-MCA vs SM IV-MCA and RM IV-MCA vs RM CV-MCA; ## P<0.05, SM IV-MCA vs SM CV-MCA; (C) Changes of HR comparison; # P<0.05, RM-HR vs SM-HR; (D) Changes of MAP comparison; # P<0.05, RM-MAP.

found that intraoperative management guided by the use of cerebral oximetry was associated with a reduction in the incidence of postoperative cognitive dysfunction and a significantly shorter length of ICU stay. Various studies reported statistically significant associations between desaturation duration and severe adverse outcome incidence [31,33]. In the present study, rSO_2 did decrease for a short time; however, whether this transient desaturation of rSO_2 has an effect on patients still needs further research, but prolonged cerebral desaturation duration during operations was revealed as an important predictor of cognitive decline and should be avoided.

The causes of the rSO_2 and V-MCA decrease still need to be discussed. RM leads to a decrease in rSO_2 and V-MCA, which may be related to intracranial pressure (ICP) and CPP. Changes in rSO_2 and V-MCA were associated with the changes in ICP

and CPP [34,35]. The change in rSO_2 is negatively correlated with the change in ICP and positively correlated with the change in CPP [36,37].

Ludwig et al [35] reported that elevated airway pressure can increase ICP and decrease CPP. Bein et al [38] investigated the effects of lung RM on ICP and cerebral metabolism in patients. The peak pressure in that study was up to 60 cmH_20 , which sustained for 30 s. RM increased ICP and decreased CPP and blood oxygen saturation of the jugular vein bulb, indicating the beginning of cerebral ischemia. However, the present study proved that a lower pressure (30 cmH₂O) also led to a reduction in rSO₂, increasing the risk of cerebral ischemia. In patients with brain lesions at an increased risk of ARDS, lung-protective ventilation contained with RM was applied to combine the treatment of hypoxemia. On the one hand, RM

Table 3A. Correlation analysis.

DM	rSO ₂ change (%)		
KIWI -	r value	<i>P</i> value	
HR change (%)	0.086	0.518	
MAP change (%)	0.720	<0.001	
PaCO ₂ change (%)	0.204	0.121	

Table 3B. Correlation analysis.

DM	V-MCA change (%)		
KIM	r value	<i>P</i> value	
HR change (%)	0.036	0.789	
MAP change (%)	0.557	<0.001	
PaCO ₂ change (%)	0.275	0.037	
rSO ₂ change (%)	0.566	<0.001	

Correlation analysis. Correlation analysis among the changes in HR, MAP, $PaCO_2$, rSO_2 , and V-MCA during the recruitment maneuver. P<0.05. HR – heart rate; MAP – mean arterial pressure; $PaCO_2$ – arterial partial pressure of carbon dioxide; RM – recruitment maneuver; rSO_2 – regional oxygen saturation; SM – sham maneuver; V-MCA – blood velocity of the middle cerebral artery.

enhanced oxygenation in patients with brain lesions; on the other hand, it increased ICP and decreased CPP [38-40]. The patients in this study performed similarly to the patients with brain injury during RM.

The high airway pressure and high tidal volume of an RM decreased cardiac output and blood pressure, increased ICP, decreased CPP, and deteriorated the intracranial blood supply [41,42]. Dynamic cerebral autoregulation and cerebrovascular carbon dioxide reactivity in CEA patients may be impaired by long-term cerebral ischemia in the area supplied by the ICA, whereby slight changes in MAP may lead to marked changes in cerebral blood flow and affect cerebral perfusion [43,44]. Relative changes of V-MCA on the ipsilateral side decreased more than the contralateral side, which might be evidence of this.

We found that there was a decrease in MAP, rSO_2 , and V-MCA during RM. Furthermore, similar to other studies, the changes in blood pressure correlated with the changes in the rSO_2 and V-MCA [45]. In addition to MAP, $PaCO_2$ affects rSO_2 and V-MCA. Mild hypercapnia dilated the cerebral blood vessels and increases cerebral blood flow and is associated with the increase in rSO_2 from the baseline [46,47]. $PaCO_2$, V-MCA, and rSO_2 were higher after SM than after RM (**Table 2**); hence, we

deduced that the changes in V-MCA and rSO₂ may be associated with the hypercapnia caused by ventilation pause. By statistical analysis, we found that the changes in PaCO₂ were not correlated with the changes in rSO₂ and V-MCA during SM. However, in the present study, there was a weak correlation between change in PaCO₂ and change in V-MCA. Because in our study we did not measure PaCO₂ directly but calculated it by the P_{ET}CO₂ during each treatment period, relationships among PaCO₂, V-MCA, and rSO₂ need further research. The decreased rSO₂ and V-MCA after RM in our study suggested that the significant change in circulation caused by the change of airway pressure was a more important factor that affects cerebral blood flow and cerebral oxygenation than the effect of carbon dioxide.

The purpose of an RM is to maintain a certain pressure for a certain period, reopen collapsed alveoli, and reduce the adverse effects of mechanical ventilation on the lungs. An often-used protocol for RM is to maintain an airway pressure of $30-40 \text{ cmH}_2\text{O}$ for 20-30 s, which seems to achieve alveolar retention without barometric injury in animal experiments; its effect on improving oxygenation in patients with ARDS has also been verified in clinical experiments [48]. In the present study, this method was used for RM. Although it was simple and effective, our results confirmed that such manipulation leads to changes in cerebral oxygen saturation and cerebral blood velocity in patients undergoing CEA. Therefore, the RM of 30 cmH₂O for 30 s should be carefully used for patients with carotid artery stenosis undergoing CEA.

All of the observed indicators returned to baseline within 5 min, but unfortunately the more accurate recovery time was not recorded. The recovery time is similar to that of another study, showing that the changes in ICP and CPP caused by RM return to the baseline value within 2-3 min [40]. NIRS and TCD are not the criterion standard in detecting ischemia for their intrinsic limitations, but their changes can be used as a trend monitor for cerebral perfusion change. Although an RM brings benefits, it also can affect cerebral perfusion. Whether transient changes in V-MCA and rSO₂ caused by an RM have long-term effects on patients needs to be further explored.

There are some limitations in this study. First, no specific time was observed for each parameter to return to the baseline value. This study proved only that all the observed parameters returned to the baseline value within 5 min. If the parameter has been recorded, the appropriate time for an RM could be determined more accurately, thus achieving pulmonary retention and minimizing its impact. Second, we recorded only the intraoperative information of this study; a long-term observation of postoperative recovery was not made. Follow-up studies should focus on whether decreased V-MCA and rSO₂ caused by an RM influence the long-term recovery of patients.

Conclusions

CEA is done to prevent a future stroke. However, owing to the particularity of the disease group and the surgery itself, the occurrence of pulmonary complications is higher for CEA than any other surgery. An RM has been occasionally used in such patients. This study revealed that the RM of 30 cmH₂O for 30 s results in hemodynamic fluctuations, reduced MAP, and decreased cerebral oxygen saturation monitored by NIRS and cerebral blood velocity by TCD. Whether these changes affect long-term prognosis is still unclear. Therefore, a study involving postoperative outcomes is needed.

References:

- 1. Howell SJ. Carotid endarterectomy. Brit J Anaesth. 2007;99:119-31
- Marinò V, Aloj F, Vargas M, et al. Intraoperative neurological monitoring with evoked potentials during carotid endarterectomy versus cooperative patients under general anesthesia technique. J Neurosurg Anesth. 2018;30:258-64
- Thirumala PD, Kumar H, Bertolet M, et al. Risk factors for cranial nerve deficits during carotid endarterectomy: A retrospective study. Clin Neurol Neurosur. 2015;130:150-54
- Kitagawa T, Ishikawa H, Yamamoto J, Ota S. Takotsubo cardiomyopathy and neurogenic pulmonary edema after carotid endarterectomy. World Neurosurg. 2019 [Online ahead of print]
- Ballotta E, Da GG, Renon L, et al. Cranial and cervical nerve injuries after carotid endarterectomy: A prospective study. Surgery. 1999;125:85-91
- Malik OS, Brovman EY, Urman RD. The use of regional or local anesthesia for carotid endarterectomies may reduce blood loss and pulmonary complications. J Cardiothor Vasc An. 2019;33:935-42
- Greene NH, Minhaj MM, Zaky AF, Rozet I. Perioperative management of carotid endarterectomy: A survey of clinicians' backgrounds and practices. J Cardiothor Vasc An. 2014;28:990-93
- 8. Ramachandran SK, Nafiu OO, Ghaferi A, et al. Independent predictors and outcomes of unanticipated early postoperative tracheal intubation after nonemergent, noncardiac surgery. Anesthesiology. 2011;115:44-53
- Brismar B, Hedenstierna G, Lundquist H, et al. Pulmonary densities during anesthesia with muscular relaxation – a proposal of atelectasis. Anesthesiology. 1985;62:422-28
- Rothen HU, Neumann P, Berglund JE, et al. Dynamics of re-expansion of atelectasis during general anaesthesia. Br J Anaesth. 1999;82:551-56
- Young CC, Harris EM, Vacchiano C, et al. Lung-protective ventilation for the surgical patient: International expert panel-based consensus recommendations. Brit J Anaesth. 2019;123:898-913
- Wei K, Min S, Cao J, et al. Repeated alveolar recruitment maneuvers with and without positive end-expiratory pressure during bariatric surgery: A randomized trial. Minerva Anestesiol. 2018;84:463-72
- Ladha K, Vidal MM, McLean DJ, et al. Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: hospital based registry study. BMJ. 2015;351:h3646
- Aretha D, Fligou F, Kiekkas P, et al. Safety and effectiveness of alveolar recruitment maneuvers and positive end-expiratory pressure during general anesthesia for cesarean section: A prospective, randomized trial. Int J Obstet Anesth. 2017;30:30-38
- Paulus F, Binnekade JM, Vroom MB, Schultz MJ. Benefits and risks of manual hyperinflation in intubated and mechanically ventilated intensive care unit patients: A systematic review. Crit Care. 2012;16:R145
- 16. Flexman AM, Gooderham PA, Griesdale DE, et al. Effects of an alveolar recruitment maneuver on subdural pressure, brain swelling, and mean arterial pressure in patients undergoing supratentorial tumour resection: A randomized crossover study. Can J Anaesth. 2017;64:626-33
- Uysal S, Lin H, Trinh M, et al. Optimizing cerebral oxygenation in cardiac surgery: A randomized controlled trial examining neurocognitive and perioperative outcomes. J Thorac Cardiovasc Surg. 2020;159:943-53

Conflict of Interest

None.

- Deschamps A, Hall R, Grocott H, et al. Cerebral oximetry monitoring to maintain normal cerebral oxygen saturation during high-risk cardiac surgery: A randomized controlled feasibility trial. Anesthesiology. 2016;124:826-36
- 19. Yun W. Cerebral monitoring during carotid endarterectomy by transcranial Doppler ultrasonography. Ann Surg Treat Res. 2017;92:105-9
- 20. Li J, Shalabi A, Ji F, Meng L. Monitoring cerebral ischemia during carotid endarterectomy and stenting. J Biomed Res. 2017;30:11-16
- 21. Denault A, Deschamps A, Murkin JM. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy. Semin Cardiothorac Vasc Anesth. 2007;11:274-81
- Pedrini L, Magnoni F, Sensi L, et al. Is near-infrared spectroscopy a reliable method to evaluate clamping ischemia during carotid surgery? Stroke Res Treat. 2012;2012:156975
- Stilo F, Spinelli F, Martelli E, et al. The sensibility and specificity of cerebral oximetry, measured by INVOS-4100, in patients undergoing carotid endarterectomy compared with awake testing. Minerva Anestesiol. 2012;78:1126
- 24. Moritz S, Kasprzak P, Arlt M, et al. Accuracy of cerebral monitoring in detecting cerebral ischemia during carotid endarterectomy: A comparison of transcranial Doppler sonography, near-infrared spectroscopy, stump pressure, and somatosensory evoked potentials. Anesthesiology. 2007;107:563-69
- Wang Y, Li L, Wang T, et al. The efficacy of near-infrared spectroscopy monitoring in carotid endarterectomy: A prospective, single-center, observational study. Cell Transplant. 2018;28:170-75
- 26. An Y, Zhao L, Wang T, et al. Preemptive oxycodone is superior to equal dose of sufentanil to reduce visceral pain and inflammatory markers after surgery: A randomized controlled trail. BMC Anesthesiol. 2019;19(1):96
- Kamenskaya OV, Loginova IY, Lomivorotov VV. Predictors of cerebral complications during carotid endarterectomy. Zh Nevrol Psikhiatr Im S S Korsakova. 2017;117:10-13
- Scheeren TWL, Schober P, Schwarte LA. Monitoring tissue oxygenation by near infrared spectroscopy (NIRS): Background and current applications. J Clin Monit Comput. 2012;26:279-87
- Sahan C, Sungur Z, Camci E, et al. Effects of cerebral oxygen changes during coronary bypass surgery on postoperative cognitive dysfunction in elderly patients: A pilot study. Rev Bras Anestesiol. 2018;68:142-48
- Sørensen H, Grocott HP, Secher NH. Near infrared spectroscopy for frontal lobe oxygenation during non-vascular abdominal surgery. Clin Physiol Funct I. 2016;36:427-35
- Colak Z, Borojevic M, Bogovic A, et al. Influence of intraoperative cerebral oximetry monitoring on neurocognitive function after coronary artery bypass surgery: A randomized, prospective study. Eur J Cardiothorac Surg. 2015;47:447-54
- Zorrilla-Vaca A, Healy R, Grant MC, et al. Intraoperative cerebral oximetrybased management for optimizing perioperative outcomes: A meta-analysis of randomized controlled trials. Can J Anaesth. 2018;65:529-42
- 33. Trafidło T, Gaszyński T, Gaszyński W, Nowakowska-Domagała K. Intraoperative monitoring of cerebral NIRS oximetry leads to better postoperative cognitive performance: A pilot study. Int J Surg. 2015;16:23-30
- 34. Kampfl A, Pfausler B, Denchev D, et al. Near infrared spectroscopy (NIRS) in patients with severe brain injury and elevated intracranial pressure. A pilot study. Acta Neurochir Suppl. 1997;70:112-14

- Ludwig HC, Klingler M, Timmermann A, et al. The influence of airway pressure changes on intracranial pressure (ICP) and the blood flow velocity in the middle cerebral artery (VMCA). Anasthesiol Intensivmed Notfallmed Schmerzther. 2000;35:141-45
- Navarro LHC, Lima RM, Khan M, et al. Continuous measurement of cerebral oxygen saturation (rSO) for assessment of cardiovascular status during hemorrhagic shock in a swine model. J Trauma Acute Care Surg. 2012;73:S140-46
- Palazón JH, Asensi PD, López SB, et al. [Effect of head elevation on intracranial pressure, cerebral perfusion pressure, and regional cerebral oxygen saturation in patients with cerebral hemorrhage.] Rev Esp Anestesiol Reanim. 2008;55:289-93 [in Spanish]
- Bein T, Kuhr LP, Bele S, et al. Lung recruitment maneuver in patients with cerebral injury: Effects on intracranial pressure and cerebral matabolism. Intens Care Med. 2002;28:554-58
- Hartland BL, Newell TJ, Damico N. Alveolar recruitment maneuvers under general anesthesia: A systematic review of the literature. Resp Care. 2015;60:609-20
- Nemer SNRP, Caldeira JBRM, Azeredo LMRM, et al. Alveolar recruitment maneuver in patients with subarachnoid hemorrhage and acute respiratory distress syndrome: A comparison of 2 approaches. J Crit Care. 2011;26:22-27
- Singer M, Vermaat J, Hall G, Latter G, Patel M. Hemodynamic effects of manual hyperinflation in critically ill mechanically ventilated patients. Chest. 1994;106:1182-87

- 42. Das A, Haque M, Chikhani M, et al. Hemodynamic effects of lung recruitment maneuvers in acute respiratory distress syndrome. BMC Pulm Med. 2017;17:34
- Hori D, Ono M, Adachi H, Hogue CW. Effect of carotid revascularization on cerebral autoregulation in combined cardiac surgery. Eur J Cardio-Thorac. 2016;49:281-87
- 44. White RP, Markus HS. Impaired dynamic cerebral autoregulation in carotid artery stenosis. Stroke. 1997;28:1340-44
- 45. Brady K, Joshi B, Zweifel C, et al. Real-time continuous monitoring of cerebral blood flow autoregulation using near-infrared spectroscopy in patients undergoing cardiopulmonary bypass. Stroke. 2010;41:1951-56
- 46. Wong C, Churilov L, Cowie D, et al. Randomised controlled trial to investigate the relationship between mild hypercapnia and cerebral oxygen saturation in patients undergoing major surgery. BMJ Open. 2020;10:e29159
- Markwalder TM, Grolimund P, Seiler RW, et al. Dependency of blood flow velocity in the middle cerebral artery on end-tidal carbon dioxide partial pressure – a transcranial ultrasound Doppler study. J Cereb Blood Flow Metab. 1984;4:368-72
- Lapinsky SE, Aubin M, Mehta S, et al. Safety and efficacy of a sustained inflation for alveolar recruitment in adults with respiratory failure. Intensive Care Med. 1999;25:1297-301