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Cerebral oxygen desaturation in patients with totally thoracoscopic ablation for atrial fibrillation

A prospective observational study

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Abstract

Background: Epicardial radiofrequency ablation for stand-alone atrial fibrillation under total video-assisted thoracoscopy has gained popularity in recent years. However, severe cardiopulmonary disturbances during the surgery may affect cerebral perfusion and oxygenation. We therefore hypothesized that regional cerebral oxygen saturation (rSO_2) would decrease significantly during the surgery. In addition, the influencing factors of rSO_2 would be investigated.

Methods: A total of 60 patients scheduled for selective totally thoracoscopic ablation for stand-alone atrial fibrillation were enrolled in this prospective observational study. The rSO_2 was monitored at baseline (T0), 15 min after anesthesia induction (T1), 15 minute after 1-lung ventilation (T2), after right pulmonary vein ablation (T3), after left pulmonary vein ablation (T4) and 15 minute after 2-lung ventilation (T5) using a near-infrared reflectance spectroscopy -based cerebral oximeter. Arterial blood gas was analyzed using an ABL 825 hemoximeter. Associations between rSO_2 and hemodynamic or blood gas parameters were determined with univariate and multivariate linear regression analyses.

Results: The rSO_2 decreased greatly from baseline 65.4% to 56.5% at T3 ($P<.001$). Univariate analyses showed that rSO_2 correlated significantly with heart rate (r=-0.173, $P=.186$), mean arterial pressure (MAP, r=0.306, $P=.018$), central venous pressure (r=0.261, $P=.044$), arterial carbon dioxide tension (r=-0.336, $P=.009$), arterial oxygen pressure (PaO_2, r=0.522, $P<.001$), and base excess (BE, r=0.316, $P=.014$). Multivariate linear regression analyses further showed that it correlated positively with PaO_2 ($\beta=0.456$, $P<.001$), MAP ($\beta=0.251$, $P=.020$), and BE ($\beta=0.332$, $P=.003$).

Conclusion: Totally thoracoscopic ablation for atrial fibrillation caused a significant decrease in rSO_2. There were positive correlations between rSO_2 and PaO_2, MAP, and BE.

Abbreviations: BE = base excess, CVP = central venous pressure, Hb = hemoglobin, HR = heart rate, Lac = lactate, MAP = mean arterial pressure, $PaCO_2$ = arterial carbon dioxide tension, PaO_2 = arterial oxygen pressure, rSO_2 = regional cerebral oxygen saturation.

Keywords: arterial oxygen pressure, atrial fibrillation, mean arterial pressure, regional cerebral oxygen saturation, surgical ablation

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

This study was approved by the institutional review board of Xinhua hospital. All patients voluntarily agreed to participate in this study and written informed consent was received from each patient the day before the surgery.

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1. Introduction

Atrial fibrillation occurs in approximately 1% to 2% of population and is associated with high incidence of stroke and heart failure.[1,2] Pharmacological antiarrhythmic and antithrombotic agents are first-line treatments for atrial fibrillation. However, these medications are often ineffective or poorly tolerated. In this case, ablation strategies including catheter ablation and surgical epicardial ablation have been developed as an alternative to medical management.[3] Compared to traditional catheter ablation, surgical ablation has gained greater interests in recent years. Two recent systematic reviews have demonstrated that surgical ablation brings higher freedom from atrial fibrillation and lower recurrence.[4,5] These advantages are more prominent for those patients with refractory atrial fibrillation and prior failed catheter intervention.

Cox-Maze III procedure constitutes the basis of surgical ablation.[6] With the progressive advances in ablation energy sources, this procedure has evolved from the traditional 'cut-and-sew' method to ablation with radiofrequency or cryothermy.[7] Furthermore, total video-assisted thoracoscopy replaces the original bilateral thoracotomy, which makes surgery minimally invasive.[8,9] The progress in ablation energy and surgical technique contributes to the popularity of epicardial ablation. However, surgical manipulations on the beating heart would cause severe hemodynamic instability and affect perfusion in peripheral tissues. In addition, the thoracoscopic ablation procedure is usually performed under 1-lung ventilation. Interferences from both cardiovascular and pulmonary systems may result in cerebral hypoperfusion and hypoxemia. Therefore, the issues of brain oxygenation insufficiency should be seriously addressed.

Regional cerebral oxygen saturation (rSO_2) is widely used for monitoring cerebral tissue oxygenation during cardiovascular and thoracic surgeries. It is reported that a decline in rSO_2 is associated with cerebral tissue hypoxemia, cognitive dysfunction and higher mortality.[10–12] Maintenance of intraoperative rSO_2 at normal levels helps reduce incidence of cognitive impairment after surgery and total mortality in the hospital. Here we tested the hypothesis that rSO_2 would decrease significantly during totally thoracoscopic ablation for atrial fibrillation. The influencing factors of rSO_2 would be also determined in this study.

2. Materials and methods

2.1. Study population

Between July 2016 and June 2018, 60 adult patients scheduled for selective totally thoracoscopic ablation for stand-alone atrial fibrillation were enrolled in this prospective observational study. Patients with concomitant chronic obstructive pulmonary disease, asthma, severe valvular heart disease, myocardial infarction, congestive heart failure, cerebral infarction, neurodegenerative diseases, psychiatric disorders, history of cardiac or lung surgery, left ventricular ejection fraction lower than 30%, left atrium more than 70 mm and left atrial appendage (LAA) thrombi were excluded. This study was approved by the institutional review board of Xinhua hospital. All patients voluntarily agreed to participate in this study and written informed consent was received from each patient the day before the surgery.

2.2. Anesthesia management

After peripheral vein cannulation, a dose of 2 mg of midazolam was intravenously injected to sedate the patients. A right-sided radial artery cannula was then implanted for monitoring arterial blood pressure and analyzing baseline blood gas condition. General anesthesia was induced with midazolam (0.05 mg/kg), etomidate (0.3 mg/kg), fentanyl (3 μg/kg) and rocuronium (0.6 to 0.9 mg/kg), followed by the insertion of a left-sided double-lumen endotracheal tube (32, 35 or 37 French, Covidien, Mansfield, MA). Anesthesia was maintained with a continuous infusion of propofol (4 to 6 $mg\,kg^{-1}\cdot h^{-1}$), remifentanil (0.15 to 0.3 $\mu g\cdot kg^{-1}\cdot min^{-1}$) and rocuronium (0.6 $mg\,kg^{-1}\cdot h^{-1}$). All patients received positive controlled ventilation with a tidal volume of 5 to 8 mL/kg and a fraction of inspired oxygen of 0.6 to 1.0, at a respiratory rate of 10 to 12 breaths/min. The thoracoscopic surgical ablation was totally conducted on the left side of chest wall. Therefore, patients were placed in the right lateral decubitus position and left lung collapse was requested. Various strategies including increasing FiO_2, endotracheal suction, adjusting position of double-lumen tube and two-lung ventilation were used if SpO_2 was lower than 90% during one-lung ventilation. Vasopressors (phenylephrine or norepinephrine) were administrated to prevent intraoperative hypotension (a mean arterial pressure [MAP] reduction of >20%). When the operation ended, patients were transferred to intensive care unit for extubation and recovery.

2.3. Cerebral rSO_2 monitoring

Cerebral rSO_2 was monitored using a near-infrared reflectance spectroscopy (NIRS)-based cerebral oximeter (EGOS-600A series, Suzhou Engin Biomedical Electronics Co., Ltd, Jiangsu, China). After cleaning the patient's skin surface with alcohol, 2 sensors were placed bilaterally on the forehead. To reduce light contamination, a black belt was used to cover the sensors during the surgery. The left and right rSO_2 were simultaneously detected at baseline (T0), 15 minutes after anesthesia induction (T1), 15 minutes after 1-lung ventilation (T2), after right pulmonary vein ablation (T3), after left pulmonary vein ablation (T4), and 15 minutes after 2-lung ventilation (T5). The average rSO_2 value was calculated at each time point.

2.4. Hemodynamic evaluation and blood gas analysis

Hemodynamic changes during the surgery were assessed at the same time points as the rSO_2. The hemodynamic measurements included heart rate (HR), MAP and central venous pressure (CVP). Concurrently, arterial blood gas was analyzed by measuring pH, arterial carbon dioxide tension ($PaCO_2$), arterial oxygen pressure (PaO_2), hemoglobin (Hb), base excess (BE) and lactate (Lac) using an ABL 825 hemoximeter (Radiometer Copenhagen, Denmark).

2.5. Surgical procedure

The procedure was performed in alignment with a previous study.[13] Briefly, bipolar radiofrequency ablation was conducted across 3 circles and 2 lines on the left atrium. Ablation of 3 circles included lesions of the right pulmonary vein (including right superior and inferior pulmonary veins), the left pulmonary vein (including right superior and inferior pulmonary veins) and the circle crossing over the left inferior pulmonary vein and the right superior pulmonary vein. Two linear ablations were referred to linear lesions from the left pulmonary vein to the left atrial appendage and from the left inferior pulmonary vein to the mitral valve annulus. Subsequently, ganglionic plexus on the epicardium was ablated and left atrial appendage was removed using a stapler.

2.6. Statistical analysis

Continuous data are presented as the mean ± standard deviation or median with interquartile range as appropriate. Categorical data are expressed as the number (percentage) of patients. The normality of continuous data was tested with Shapiro–Wilk method. Comparisons of rSO_2, hemodynamic and laboratory parameters at different time points were performed using a one-way repeated-measures ANOVA followed by post hoc Bonferroni analysis if the data met the assumption of normality, or nonparametric Friedman test would be applied. If rSO_2 showed significant differences at a specific time point, a univariate analysis was performed to illustrate possible influencing factors of rSO_2 with Pearson or Spearman correlations. The variables with P value less than .2 were further incorporated into a multivariate linear regression analysis (stepwise method). Statistical significance was considered if P value was less than

.05. All the statistical analyses were conducted using IBM SPSS software version 20 (SPSS Inc., Chicago, IL).

3. Results

Table 1 illustrated demographic and clinical characteristics of patients. A total of 60 patients consisting of 34 male and 26 female patients were included in this study. Among these patients, the average age was 62±8 years. Thirty-four patients (70%) were diagnosed as paroxysmal atrial fibrillation, 7 patients (18%) had persistent atrial fibrillation, and four patients (12%) had longstanding persistent atrial fibrillation. The mean (SD) left atrial dimension and left ventricular ejection fraction were 42.3±4.9 mm and 61.5%±4.2%, respectively. The majorities of patients had various comorbidities and took different types of medicines.

Regarding rSO_2, there were significant differences among the six time points ($P < .001$, one-way repeated-measures ANOVA) (Fig. 1). The rSO_2 decreased from baseline 65.4% to the lowest 56.5% at T3 ($P < .001$, post hoc Bonferroni test), which meant that right pulmonary vein ablation caused a significant decrease in rSO_2. A 1-way repeated-measures ANOVA or Friedman test revealed that significant differences were observed among six time points in term of hemodynamic parameters, including HR ($P = .008$), MAP ($P < .001$) and CVP ($P < .001$). The blood gas analysis showed similar characteristics. There were significant differences among six time points in pH ($P < .001$), $PaCO_2$ ($P < .001$), PaO_2 ($P < .001$), Hb ($P < .001$), BE ($P < .001$) and Lac ($P < .001$) (Table 2). These results suggested that surgical ablation of atrial fibrillation led to intensive disturbances in the hemodynamic and blood gas variables.

Univariate analyses showed that rSO_2 was correlated significantly with HR (r=-0.173, $P = .186$), MAP (r=0.306, $P = .018$), CVP (r=0.261, $P = .044$), $PaCO_2$ (r=-0.336, $P = .009$), PaO_2 (r=0.522, $P < .001$), and BE (r=0.316, $P = .014$) (Table 3). However, there were no correlations between rSO_2 and other variables including pH, Hb, and Lac. The variables screened in the univariate analysis were further included for multivariate linear regression analysis. We found that there were significant positive correlations between rSO_2 and PaO_2 ($\beta = 0.456$, $P < .001$), MAP ($\beta = 0.251$, $P = .020$), and BE ($\beta = 0.332$, $P = .003$).

Table 1

Demographic and clinical characteristics of patients.

Gender, male/female, No.	34/26
Age, yr	62±8
Weight (kg)	65±8
Height (cm)	163±6
BMI (kg/m^2)	24±2
Classification of atrial fibrillation (AF), No. (%)	
Paroxysmal AF	42 (70)
Persistent AF	11 (18)
Longstanding persistent AF	7 (12)
LAD (mm)	42.3±4.9
LVEF (%)	61.5±4.2
NYHA class, No. (%)	
I	12 (20)
II	40 (67)
III	8 (13)
ASA physical status, No. (%)	
I–II	49 (82)
III	11 (18)
Comorbidies, No. (%)	
Hypertension	19 (32)
Coronary heart disease	9 (15)
Obstructive sleep apnea	8 (13)
Diabetes mellitus	11 (18)
History of smoking	21 (35)
History of catheter ablation	13 (22)
Medications, No. (%)	
Anti-arrhythmic drugs	
Amiodarone	18 (30)
Digoxin	12 (20)
β-Blockers	21 (35)
Calcium channel blockers	15 (25)
Anticoagulants, No. (%)	
Warfarin	11 (18)
Aspirin	14 (23)
Clopidogrel	8 (13)
ACEI or ARB, No. (%)	16 (26)
Diuretics, No. (%)	19 (31)

Data were presented as mean ± standard deviation or the number (percentage) of patients. ACEI=angiotensin-converting enzyme inhibitors, ARB=angiotensin receptor blocker, ASA physical status=American Society of Anesthesiologists physical status, BMI=body mass index, LAD=left atrial diameter, LVEF=left ventricular ejection fraction, NYHA=New York Heart Association.

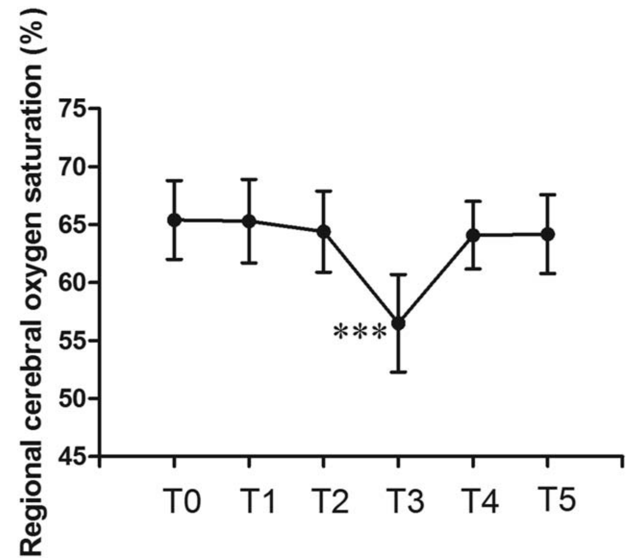

Figure 1. Time course of rSO_2 changes during the surgery. $^{***}P < .001$ vs T0. rSO_2=regional cerebral oxygen saturations. T0=at baseline.

4. Discussion

The present study supported the hypothesis that rSO_2 would decrease significantly during totally thoracoscopic ablation for atrial fibrillation. Furthermore, we found that rSO_2 correlated positively with PaO_2, MAP and BE. However, no significant correlations were observed between rSO_2 and other hemodynamic and blood gas variables including HR, CVP, pH, $PaCO_2$, Hb, Lac.

We found that rSO_2 decreased mainly at two time points: after right pulmonary vein ablation and after left pulmonary vein ablation. However, a significant decrease in rSO_2 was only seen after right pulmonary vein ablation. This result could be partly explained by surgical disturbances. The operation was performed through the left thoracic cavity. Most of pulmonary blood flow

Table 2

rSO_2 and hemodynamic changes at 6 time points of surgery.

	T0	T1	T2	T3	T4	T5
rSO_2 (%)	65.4±3.4	65.3±3.6	64.4±3.5	56.5±6.1***	64.1±2.9	64.2±3.4
HR (bpm)	79 (67, 92)	65 (56,78)***	70 (63, 82)	73 (63, 89)	77 (67, 89)	77 (72, 83)
MAP (mm Hg)	95±14	74±12***	77±12***	43±8***	65±8***	79±8***
CVP (cm H_2O)	6 (5, 8)	8 (6, 11)*	12 (9, 15)***	7 (6, 9)	13 (11, 18)***	13 (12, 16)***
Ph	7.42±0.02	7.40±0.04**	7.38±0.05***	7.33±0.06***	7.35±0.05***	7.38±0.05***
$PaCO_2$ (mm Hg)	39±3	40±4	43±5**	50±8***	47±6***	42±5
PaO_2	80±8	356±88***	119±69***	61±9***	115±39***	309±92***
Hb (g/L)	14.8±1.5	14.3±1.5***	14.2±1.5***	14.0±1.6***	13.9±1.6***	13.6±1.4***
Lac (mmol/L)	1.8 (1.4, 2.1)	1.8 (1.2, 2.1)	1.8 (1.4, 2.1)	2.3 (1.7, 2.6)*	2.3 (1.7, 2.8)*	2.6 (1.9, 3.0)***
BE (mmol/L)	−0.6 (−1.4, 1.1)	−0.6 (−1.4, 1.1)	−0.3 (−1.9, 0.8)	−1.5 (−2.8, −0.4)**	−1.6 (−2.5, −0.5)*	−2.1 (−2.5, −0.8)***

Data were presented as mean ± standard deviation or median with interquartile range. BE = base exces, CVP = central venous pressure, Hb = hemoglobin, HR = heart rate, Lac = lactate, MAP = mean arterial pressure, $PaCO_2$ = arterial carbon dioxide tension, PaO_2 = arterial oxygen pressure, rSO_2 = regional cerebral oxygen saturations. T0 = at baseline; T1 = 15 min after anesthesia induction; T2 = 15 min after one-lung ventilation; T3 = after right pulmonary vein ablation; T4 = after left pulmonary vein ablation; T5 = 15 min after two-lung ventilation.

* $P<.05$.

** $P<.01$.

*** $P<.001$ vs T0.

was gravitationally redistributed into right lung when the patients were placed in the right lateral position.[14] Hypoxic pulmonary vasoconstriction of the nonventilated left lung further increased right lung perfusion.[15] Consistent with previous studies,[16,17] the right-lung ventilation during the surgery enabled patients to maintain adequate ventilation/perfusion ratio and tissue oxygenation. Once the right pulmonary vein was clamped, oxygenated forward blood flow was totally stopped. Perfusion and oxygenation in peripheral organs, especially the brain, decreased dramatically and cerebral rSO_2 showed a remarkable reduction in value. However, significant rSO_2 changes were not observed at the step of clamping the left pulmonary vein, which is partly in alignment with a previous literature reporting that left pneumonectomy did not induce hypoxemia during the surgery.[18] This observation was probably illustrated by the fact that the left lung was not ventilated. Blood flow blockade in the left pulmonary vein did not cause a severe decrease in brain tissue oxygen supply.

Oxygen and carbon dioxide are 2 important components in the blood that affect cerebral oxygenation performance. Our study showed that a positive correlation was observed between rSO_2 and PaO_2, which is consistent with previous studies stating that augmenting PaO_2 by raising FiO_2 could increase rSO_2.[19–21]

Table 3

Associations between rSO_2 and hemodynamic and laboratory parameters.

	Univariate regression		Multivariate regression	
	r	*P*	β	*P*
PaO_2	0.522	< .001	0.456	< .001
MAP	0.306	.018	0.251	.020
BE	0.316	.014	0.332	.003
HR	–0.173	.186		
CVP	0.261	.044		
pH	0.043	.745		
$PaCO_2$	–0.336	.009		
Hb	–0.116	.379		
Lac	–0.099	.452		

BE = base exces, CVP = central venous pressure, Hb = hemoglobin, HR = heart rate, Lac = lactate, MAP = mean arterial pressure, $PaCO_2$ = arterial carbon dioxide tension, PaO_2 = arterial oxygen pressure, rSO_2 = regional cerebral oxygen saturations.

Interestingly, a study enrolling patients with severe traumatic brain injury reported that rSO_2 elevation after increasing arterial oxygenation occurred in the cerebral hemisphere with impaired cerebral autoregulation.[22] The role of cerebral autoregulation in our study should be confirmed in future. Although we found that there was a positive correlation between rSO_2 and $PaCO_2$, it did not reach a significant difference. This is contradictory to several studies reporting that increasing $PaCO_2$ improved brain blood flow and rSO_2.[23–25] The reasons may come from two points. First, the effects of $PaCO_2$ on rSO_2 performance may be relatively small. It is proved that cerebral oxygenation had a slight decline during general anesthesia when normocarbia was transferred to hypocarbic conditions.[25] Second, previous prospective studies[23–25] set the same conditions and investigated single effects of $PaCO_2$ on rSO_2 changes, while our study investigated all possible influencing factors of rSO_2. The increases in rSO_2 associated with an increase in $PaCO_2$ may be offset by PaO_2 reduction.

Our study showed that there was a significant positive correlation between rSO_2 and MAP, which is consistent with previous studies.[26–28] Hunt et al[26] reported that a reduction in regional cerebral blood oxygenation was dependent on severity of hypotension during spinal anesthesia for cesarean section. Michelet et al[27] further revealed that a decrease of MBP more than 44.5% could predict a probability of cerebral desaturation >90% during surgery in neonates and infants. However, 2 other studies made a contradictory association of cerebral oxygenation with MAP.[29,30] Holmgaard et al[29] reported that vasopressors-induced higher MAP inversely led to lower mean rSO_2 during cardiopulmonary bypass in cardiac surgery. However, this result was based on a secondary outcome from the other randomized clinical trial.[31] Lucas et al[30] reported that pharmacological-induced hypotension resulted in unexpected elevated cerebral oxygenation in healthy humans. In this study, cerebral oxygenation was defined as cortical oxygenation index, but not rSO_2 in our study. What is more important, previous studies had proved that the correlation between rSO_2 and MAP was poor in non-anesthetized healthy volunteers with intact cerebral autoregulation.[26,32]

There were limitations in this study. Although NIRS-based cerebral oximeter has advantages of monitoring cerebral oxygenation noninvasively and continuously, some drawbacks should not be ignored. First, NIRS-based cerebral oximeter cannot measure global cerebral oxygenation. NIRS devices only detect oxygen saturation in a thin superficial layer (generally 2 cm) of brain tissues. The rSO_2 changes in deep brain tissues cannot be measured. Second, NIRS-based rSO_2 values reflect combined results of oxygen supply and demand in brain tissues. They cannot differentiate between arterial and venous blood.[33] Third, extracranial contamination from subcutaneous tissue, blood flow and Hb concentration will influence accuracy of rSO_2 measurement.[34] These disadvantages block NIRS-based cerebral oximeter as an accurate tool to monitor brain oxygenation in clinical circumstances.

Furthermore, cerebral oximeter sensor and patient positioning also affect rSO_2 readings during the surgery. It is reported that the rSO_2 value at the upper forehead is smaller than that at the lower forehead.[35] In the lateral position, the rSO_2 of the upper hemisphere is higher than that of the lower hemisphere.[36] However, we used a black belt to fix the sensors during the surgery. We also calculated average rSO_2 from both upper and lower hemispheres. As a result, the rSO_2 at baseline and after placement of lateral position was similar to those described in previous studies.[19,37]

In addition, transcranial Doppler ultrasound was not applied to measure cerebral blood flow in our study. Comprehensive measurements combining rSO_2 and transcranial Doppler ultrasound would be used to better reflect brain perfusion and oxygenation. However, transcranial Doppler does not easily provide continuous measurements during the surgery.

Finally, we recruited limited number of patients scheduled for selective totally thoracoscopic ablation for stand-alone atrial fibrillation. Lack of efficient subjects may bias the precision of results in this prospective observational study. More multicenter clinical trials with large samples should be performed in future.

In conclusion, our study showed for the first time that the rSO_2 decreased dramatically during totally thoracoscopic ablation for atrial fibrillation. There were positive correlations between rSO_2 and PaO_2, MAP, and BE.

Author contributions

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