Relationship between post-operative cognitive dysfunction and regional cerebral oxygen saturation and β-amyloid protein[*]

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Abstract: Objective: To investigate the relationship between post-operative cognitive dysfunction (POCD) and regional cerebral oxygen saturation (rSO_2) and β-amyloid protein (Aβ) in patients undergoing laparoscopic pancreaticoduodenectomy. Methods: Fifty patients undergoing elective laparoscopic pancreaticoduodenectomy received five groups of neuropsychological tests 1 d pre-operatively and 7 d post-operatively, with continuous monitoring of rSO_2 intra-operatively. Before anesthesia induction (t_0), at the beginning of laparoscopy (t_1), and at the time of pneumoperitoneum 120 min (t_2), pneumoperitoneum 240 min (t_3), pneumoperitoneum 480 min (t_4), the end of pneumoperitoneum (t_5), and 24 h after surgery, jugular venous blood was drawn respectively for the measurement of Aβ by enzyme-linked immunosorbent assay (ELISA). Results: Twenty-one cases of the fifty patients suffered from POCD after operation. We found that the maximum percentage drop in rSO_2 ($rSO_{2, \%max}$) was significantly higher in the POCD group than in the non-POCD group. The $rSO_{2, \%max}$ value of over 10.2% might be a potential predictor of neurocognitive injury for those patients. In the POCD group, the plasma Aβ levels after 24 h were significantly higher than those of pre-operative values ($P<0.01$). After 24 h, levels of plasma Aβ in the POCD group were significantly higher than those in the non-POCD group ($P<0.01$). Conclusions: The development of POCD in patients undergoing laparoscopic pancreaticoduodenectomy is associated with alterations of rSO_2 and Aβ. Monitoring of rSO_2 might be useful in the prediction of POCD, and Aβ might be used as a sensitive biochemical marker to predict the occurrence of POCD.

Key words: Laparoscopic pancreaticoduodenectomy, Regional cerebral oxygen saturation, β-Amyloid protein, Post-operative cognitive dysfunction

doi:10.1631/jzus.B1400130　　　　　**Document code:** A　　　　　**CLC number:** R74; R446.11[+]2

1 Introduction

The incidence of early post-operative cognitive dysfunction (POCD) can reach as high as 40%–50%, which adversely affects quality of life and rehabilita-

tion of patients (Rohan *et al.*, 2005). The underlying pathophysiological mechanism of POCD remains unclear.

Alzheimer's disease (AD) is a chronic progressive neurologic degeneration. Recent studies have shown that prolonged POCD increases the incidence of dementia (Vanderweyde *et al.*, 2010; Bittner *et al.*, 2011). Fodale *et al.*, (2010) thought that the pathological mechanism of POCD is similar to that of AD. Also, the type of operation and anesthesia, differences in genes, central cholinergic system, β-amyloid

protein (Aβ), cholinergic system, older age, and anesthetics may also have impact on the development of POCD.

The possible risk factors contributing to the development of POCD include age, pre-operative cognitive function, operation time, hypoperfusion, embolism, post-operative pain, respiratory complications, and infections (Krenk *et al.*, 2010). The proposition of intervention includes cerebral oxygen saturation monitoring and the control of the depth of anesthesia. In non-cardiac surgery, monitoring of regional cerebral oxygen saturation (rSO_2) has been proven to be important for improving the results of intervention factors (Casati *et al.*, 2005; Farag *et al.*, 2006; Slater *et al.*, 2009).

Transcranial near-infrared spectroscopy (NIRS) provides a non-invasive method to detect rSO_2. Recent studies have shown that the development of POCD had a significant relationship with the levels of rSO_2 in patients undergoing coronary artery bypass graft (CABG) (Olsen *et al.*, 1996; Murkin *et al.*, 2007). The studies using NIRS have shown that there was a significant relationship between low rSO_2 and neurologic complications, cognitive function, and prolonged hospitalization for the patients undergoing abdominal operation or CABG surgery under anesthesia (Monk *et al.*, 2002; Goldman *et al.*, 2004; Yao *et al.*, 2004; Casati *et al.*, 2005).

Laparoscopic pancreaticoduodenectomy has been widely used with reduced hospitalization time, fast recovery, and improved quality of life for patients. However, it also has some shortcomings; for example, compared with a conventional operation, its average operation time is up to 10 h, average blood loss 139 ml, post-operation hospitalization time up to 6.6 d (Jacobs and Kamyab, 2013; Mesleh *et al.*, 2013), and the incidence of cognitive dysfunction is higher than that of other abdominal surgery. It might have a strong relationship with operation time and anesthesia management.

In this study, we detected rSO_2 and compared it with changes of plasma Aβ levels to explore the relationship between post-operative cognitive function and rSO_2 and plasma Aβ for the patients undergoing laparoscopic pancreaticoduodenectomy. We hypothesize that the changes of Aβ levels and rSO_2 would be predictive factors for POCD in patients following this operation with general anesthesia.

2 Materials and methods

2.1 Materials

This study was approved by the Ethics Committee of Linyi City People's Hospital, China and obtained informed consent of all patients. Fifty patients, American Standards Association (ASA) classes II–III, were recruited from our hospital; they received laparoscopic pancreaticoduodenectomy from December 2010 to May 2013. There were 29 males and 21 females. The age range was 40 to 80 years old. Pre-operative imaging showed that there were 30 cases of pancreatic cancer affecting the body of the pancreas and 20 cases affecting the pancreatic tail. We abided by the following exclusion criteria: (1) pre-operative mini-mental state examination (MMSE) score less than 24; (2) a current or past history of psychiatric disorder or central nervous system disease; (3) a history of cardiovascular surgery or craniotomy; (4) drug or alcohol dependence; (5) hepatic failure; (6) renal failure; (7) inability to read or speak; and, (8) serious hearing or vision impairment (Lin *et al.*, 2013).

2.2 Anesthetic management

All patients received a standardized anesthetic management. In the operating room, 5-ECG leads were attached, with leads II and V_5 continuously monitored. A 20-G radial artery catheter was inserted to measure arterial blood pressure and arterial blood gas. A 7-Fr vein catheter introducer was inserted into the right internal jugular for mixed venous oxygen saturation (SvO_2) monitoring (Hong *et al.*, 2008) and for blood sample collection to be used for Aβ assay. Three electrodes connected with Narcotrend® monitor (Narcotrend®-Compact, MT Monitor Technik GmbH und Co. KG, Germany) and an rSO_2 sensor connected with NIRS (INVOS 5100B, Somanetics, Troy, MI, USA) were placed on the skin of the forehead to separately record values of Narcotrend and rSO_2 at 30-s intervals during surgery (Lin *et al.*, 2013). After 5 min for equilibrium, Narcotrend and rSO_2 readings were regarded as the baseline values.

Anesthesia was induced with midazolam 0.04–0.05 mg/kg, propofol 1.0–1.5 mg/kg, sufentanil 1.0–1.5 μg/kg, *cis*-atracurium 0.10–0.15 mg/kg. After intubation, all patients were administered with propofol 2–5 μg/(kg·h), remifentanil 0.5–1.0 μg/(kg·min), *cis*-atracurium 2–4 μg/(kg·min), and inhalation of

sevoflurane (1%–3%). The intra-operative blood pressure and heart rate were maintained to allow fluctuation less than 30% of the baseline values. The Narcotrend index was kept between D_1 and E_1. All anesthesia-related data including dose of anesthetic agents, fluid input quantity, blood loss, the duration of operation and anesthesia, and recovery time were recorded routinely (Lin *et al.*, 2013).

2.3 Physiologic variables

Physiologic variables including SvO_2, arterial partial pressure of carbon dioxide ($PaCO_2$), arterial partial pressure of oxygen (PaO_2), glucose, and hematocrit were measured. The observation time points include: before induction of anesthesia (t_0), before the start of pneumoperitoneum (t_1), pneumoperitoneum 120 min (t_2), pneumoperitoneum 240 min (t_3), pneumoperitoneum 480 min (t_4), pneumoperitoneum end (t_5), and 24 h after surgery. A Radiometer ABL800 automatic blood gas analyzer was used for blood gas analysis.

2.4 Monitoring rSO_2

The rSO_2 was detected by NIRS (Brawanski *et al.*, 2002) using a near-infrared light spectrum analyzer INVOS5100 (Somaneti, USA). The rSO_2 probe was placed on the right side of the forehead. The instrument can monitor continuously, record, and save the oxygen data automatically. The cerebral oxygen data were recorded twice per minute. These data were transferred to a computer for statistical processing after operation (Hong *et al.*, 2008). Surgeons and anesthesiologists were blinded to the patients' group assignment and the measurement of rSO_2 so as to exclude subjective bias.

2.5 Analysis of plasma Aβ

Plasma levels of the Aβ were analyzed as a biomarker of brain injury. Blood samples were taken from participants at baseline and 1 d post-operatively. Five-ml jugular vein blood was collected into a procoagulant polyvinyl chloride (PVC) tube and placed in the refrigerator for 2 h, and then centrifuged at 3000 r/min at 4 °C for 10 min to separate the serum. The supernatant was placed in a PVC tube and placed in cryogenic refrigerator at below −20 °C. The experimental specimens were set at room temperature before reconstitution and use. The Beta Amyloid 42 ELISA Kit was used (Covance Princeton, New Jersey, USA) and the assay was performed according to the instructions provided by the supplier to establish a standard curve; measured specimen OD values were calculated to obtain the protein content.

2.6 Neurologic and neuropsychological assessments

All eligible patients underwent a battery of clinical quantitative neurologic and neuropsychological tests on the day before operation and 7 d after operation. The control group did the same tests on the same days. The battery primarily focused on memory, learning, attention, executive functions, and cognitive flexibility, and encompassed the following tests: MMSE, digit symbol substitutions test (DSST), trail making test (part A), verbal fluency test (VFT), and word recognition memory tests. The same physician carried out the evaluation of cognitive function among patients and controls according to the methods of Lin *et al.* (2013). Learning effects were defined as mean variation of each test from baseline among control subjects. The tests were performed according to the International Study of Postoperative Cognitive Dysfunction (ISPOCD1 and ISPOCD2) (Moller *et al.*, 1998; Johnson *et al.*, 2002; Canet *et al.*, 2003).

A Z score for each individual test was calculated by comparing with baseline scores and with test results one week after surgery, by subtracting the average learning effect from these changes, and being divided by the standard deviation (SD) of the control group. POCD was defined as Z scores equal to or greater than 1.96 on at least two tests (Moller *et al.*, 1998; Johnson *et al.*, 2002; Canet *et al.*, 2003; Lin *et al.*, 2013).

2.7 Statistical analysis

Statistical analysis was performed using SPSS 19.0 (IBM, Armonk, NY, USA). Continuous variables were expressed as mean±SD and processed with Student's *t*-test. Categorical variables were expressed as numbers (percentages) and processed with chi-square test or Fisher exact tests. Multivariate analysis of predictors for POCD was assessed with logistic regression. A P value less than 0.05 was considered statistically significant.

3 Results

3.1 Incidence of POCD

The clinical and demographic characteristics of the 50 patients and the comparison between POCD and non-POCD are presented in Table 1. Only 46 patients of the 50 performed the early cognitive post-test (2 patients did not participate the neurologic or neuropsychological tests, 2 patients were transferred to open pancreaticoduodenectomy). Of these 46 patients, 21 (45.7%) showed early POCD because of the Z score ≥ 1.96. Advanced age and lower education level were significant pre-operative predictors for POCD (Hong *et al.*, 2008). Basal body temperature was significantly higher in the POCD patients than in normal patients.

Table 1 Demographic and intra-operative data of the POCD and non-POCD groups

Variable	Non-POCD ($n=25$)	POCD ($n=21$)	P
Age (year)	65±5	73±3	0.010
Male/female	8/17	6/15	0.529
Height (cm)	164±4	161±5	0.135
Weight (kg)	62±6	61±5	0.611
Body mass index	23.1±2.5	23.4±1.3	0.674
Education level (year)	11±2.55	8±2.65	0.030
ASA physical status			
II (%)	48	47.6	0.607
III (%)	52	52.4	
Pre-operative complication			
Hypertension (%)	44	28.6	0.363
Diabetes (%)	24	19.0	0.735
Smoking history (%)	32	23.8	0.744
Surgical history (%)	48	47.6	0.493
Duration of anesthesia (min)	562±30	553±21	0.230
Duration of surgery (min)	530±30	524±22	0.493
Fluid replacement (ml)	4480±157	4524±162	0.189
Blood loss (ml)	141±18	149±21	0.198
Recovery time (min)	32±5.2	35±5.1	0.079
Propofol (mg)	2117.2±7.9	2112.4±8.3	0.051
Remifentanil (mg)	6.51±0.13	6.60±0.19	0.062
cis-Atracurium (mg)	27.5±2.66	28.9±2.59	0.082
T_a (°C)	36.5±0.27	36.9±0.3	<0.001

Data are presented as mean±SD or the percentage of all patients. ASA: American Society of Anesthesiologists; T_a: axillary temperature

3.2 Neurologic and neuropsychological tests

Peri-operative congnitive function test scores are shown in Table 2. In the POCD group, post-operative scores of MMSE, DSST, and VFT were significantly lower than those at baseline ($P<0.05$). Patients with POCD showed significant deterioration in learning and memory abilities and performance functional disorder, and were more anxious and depressed than non-POCD patients.

Table 2 Neuropsychological test results of the POCD and non-POCD groups

Test	Score or time (s)		P
	Non-POCD ($n=25$)	POCD ($n=21$)	
MMSE			
Pre-operative	29.00±0.67	29.30±0.34	0.054
Pod#7	28.83±0.68	27.10±0.41[*,**]	<0.001
DSST			
Pre-operative	32.32±4.75	31.00±4.23	0.329
Pod#7	29.96±4.86	26.14±3.13[*,**]	0.003
Trail making test A (s)			
Pre-operative	17.60±5.68	19.40±5.62	0.289
Pod#7	17.84±6.06	20.50±5.86	0.140
VFT			
Pre-operative	16.70±1.77	16.01±1.58	0.180
Pod#7	16.35±1.85	14.51±1.71[*,**]	<0.001
Word recognition memory test			
Pre-operative	1.20±0.44	1.30±0.48	0.689
Pod#7	1.40±0.43	1.90±0.42	0.965

The test results (scores, except time (s) for trail making test A) are presented as mean±SD. Pod#7: post-operative Day 7; MMSE: mini-mental state examination; DSST: digit symbol substitutions test; VFT: verbal fluency test. [*] $P<0.05$, vs. non-POCD group; [**] $P<0.05$, vs. baseline in either group

3.3 Physiologic variables

$PaCO_2$ was significantly higher at t_3 and t_4 in the POCD patients than in normal patients. PaO_2 was significantly higher at t_1 to t_4 than at t_0 in all patients. Remaining variables including SvO_2, glucose, and hematocrit did not significantly differ between groups (Table 3).

3.4 Comparison of rSO_2

There were no statistical differences of rSO_2, mean rSO_2 ($\overline{rSO_2}$), or minimum rSO_2 ($rSO_{2, min}$) between the two groups at baseline. Compared with the non-POCD group, maximum percentage drop in rSO_2 ($rSO_{2, \%max}$) was observably greater in the POCD group ($P=0.001$) (Table 4).

Table 3 Comparison of physiologic variables between the POCD and non-POCD groups

Time	SvO_2 (%)		$PaCO_2$ (mmHg)		PaO_2 (mmHg)		Glucose (mg/dl)		Hematocrit (%)	
	Non-POCD	POCD	Non-POCD	POCD	Non-POCD	POCD	Non-POCD	POCD	Non-POCD	POCD
t_0	81±13	83±9	33±6	34±4	277±56	267±66	123±26	115±20	30±7	31±6
t_1	78±10	80±11	37±7	37±6	361±54	341±34	152±68	162±63	29±5	28±6
t_2	75±9	78±9	38±8	39±8	362±31	342±38	206±62	216±72	27±6	26±7
t_3	73±6	76±7	43±7	49±6*	358±52	341±42	208±57	220±68	26±5	25±8
t_4	72±7	73±8	45±6	51±7*	340±33	336±28	212±49	214±52	25±8	23±5
t_5	78±9	79±10	36±8	40±6	279±76	249±80	133±36	124±34	24±8	23±8

Data are presented as mean±SD; SvO_2: mixed venous oxygen saturation; $PaCO_2$: arterial partial pressure of carbon dioxide; PaO_2: arterial partial pressure of oxygen. * $P<0.05$, vs. non-POCD group

Table 4 Comparison of baseline rSO_2, $\overline{rSO_2}$, $rSO_{2,\,min}$, and $rSO_{2,\,\%max}$ between the POCD and non-POCD groups

Group	Baseline (%)	$\overline{rSO_2}$ (%)	$rSO_{2,\,min}$ (%)	$rSO_{2,\,\%max}$ (%)
Non-POCD (n=25)	69 (67–71)	71 (69–74)	62 (59–64)	8.64 (6.7–12.0)
POCD (n=21)	69 (63–75)	69 (61–76)	59 (52–66)	13 (8.3–18.5)*
P	0.855	0.427	0.445	<0.001

Data are presented as median (5th–95th percentile). rSO_2: regional cerebral oxygen saturation; $\overline{rSO_2}$: mean rSO_2; $rSO_{2,\,min}$: minimum rSO_2; $rSO_{2,\,\%max}$: maximum percentage drop in rSO_2. * $P<0.05$, vs. non-POCD group

Fig. 1 rSO_2 trends in the POCD and non-POCD groups

Fig. 1 is a line chart of patients' intra-operative rSO_2 trends of the two groups. The rSO_2 values of the two groups at different time points were statistically significantly different ($P<0.05$). In contrast, the trends of intra-operative rSO_2 values were similar in the two groups.

$rSO_{2,\,\%max}$ was observably greater in the POCD group ($P<0.01$). Fig. 2 displays receiver operating characteristic (ROC) curve of $rSO_{2,\,\%max}$, and the area under the curve (AUC) of which was 0.926 (95% confidence interval (CI) [0.842, 1.000]). When $rSO_{2,\,\%max}>10.2\%$ was taken as the cut-off value, the specificity and sensitivity of $rSO_{2,\,\%max}$ in predicting POCD were 88.0% and 85.7%, respectively.

3.5 Aβ levels

In the POCD group, the plasma Aβ levels after 24 h were statistically significantly higher than pre-operative values ((100.27±6.79) pg/ml vs. (78.90± 11.07) pg/ml; $P<0.01$). After 24 h, the levels of plasma Aβ in the POCD group were significantly higher than those in the non-POCD group ((100.27±6.79) pg/ml vs. (78.23±11.16) pg/ml; $P<0.01$) (Table 5).
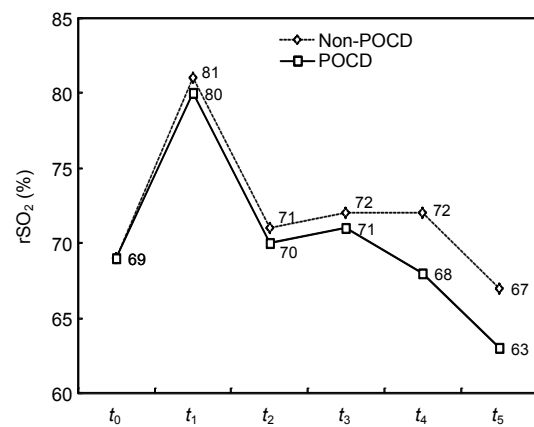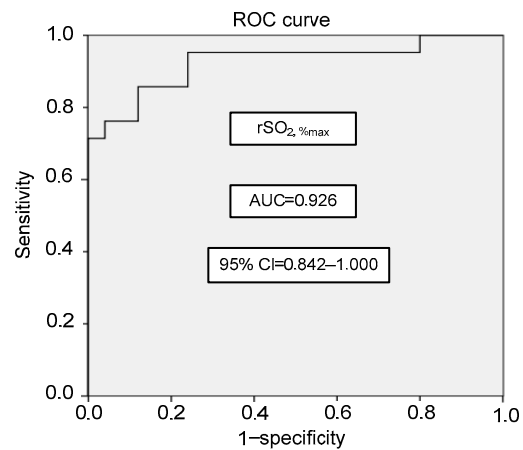

Fig. 2 Receiver operating characteristic (ROC) curves of $rSO_{2,\,\%max}$
AUC: area under the curve; CI: confidence interval

Results from risk factor analysis are presented in Table 6. In a multivariate logistic regression analysis, higher levels of basal body temperature, $rSO_{2,\,\%max}$, $PaCO_2$, and Aβ were significant intra-operative predictors for POCD.

Table 5 β-Amyloid protein (Aβ) levels of the POCD and non-POCD groups

Time	Aβ level (pg/ml)		P
	Non-POCD (n=25)	POCD (n=21)	
t_0	78.11±11.25	78.90±11.07	0.990
t_1	78.24±9.31	83.98±9.83	0.076
t_2	79.11±11.60	85.28±9.73[**]	0.060
t_3	80.72±11.55	90.88±9.66[*,**]	0.003
t_4	89.65±10.73[**]	101.70±9.25[*,**]	<0.001
t_5	91.23±11.33[**]	114.57±10.27[*,**]	<0.001
24 h	78.23±11.16	100.27±6.79[*,**]	<0.001

Data are presented as mean±SD. [*] P<0.05, vs. non-POCD group; [**] P<0.05, vs. baseline in either group

Table 6 Analysis of risk factors to POCD

Variable	OR (95% CI)	P
Age	0.305 (1.135–2.865)	0.052
Gender	0.021 (0.288–0.369)	0.807
Level of education	0.087 (0.021–1.979)	0.236
Basal body temperature	0.391 (1.539–2.461)	0.002
$PaCO_2$	0.425 (1.447–2.553)	0.005
$rSO_{2,\ \%max}$	0.794 (0.056–0.103)	<0.001
Aβ	0.577 (0.020–0.033)	<0.001

OR: odds ratio; CI: confidence interval

4 Discussion

POCD is a common post-anesthetic neurologic complication, manifested as mental confusion, anxiety, personality changes, and memory impairment. The pathogenesis of POCD is not clear, although it can be influenced by many factors. Most researchers think that POCD is related with age, operation, anesthesia, psychologic factors, sleeping disorder, and pain. There is no consistent outlook about POCD from the literature. The review reported by ISPOCD1 in 1998 was generally accepted. The incidence of POCD from 1218 elderly patients undergoing operation was 25.8% (Moller *et al.*, 1998). In the study of Evered *et al.* (2011), the incidence of POCD at 7 d post-operation from 644 patients with CABG or total hip joint replacement (THJR) was 43% and 17%, respectively. Rasmussen *et al.* (1999) observed that 17 elderly patients (≥60 years) from 35 cases who received abdominal operation with general anesthesia developed POCD (48.6%).

In our study, the incidence of POCD with laparoscopic pancreaticoduodenectomy was up to 45.7%. The risk factors included advanced age and lower level education. These results are similar to other findings (Hong *et al.*, 2008; de Tournay-Jetté *et al.*, 2010). Interestingly, higher basal body temperature might be a significant predictor for POCD based on multivariate logistic regression analysis. Whether the patients with higher basal body temperature were in a proinflammatory state or a pronounced systemic inflammation pre-operatively was not assessed in this study. Regarding the relationship between metabolic imbalance caused by systemic inflammatory reaction and psychomotor slowing (Bokeriia *et al.*, 2005), further evaluation of the effect of peri-operative inflammatory state and body temperature on POCD seems to be required (Hong *et al.*, 2008). The development of POCD may be associated with operation, anesthesia type, evaluation methods of POCD, and diagnostic criteria. In addition, small sample size may also lead to bias of the incidence.

Laparoscopic pancreaticoduodenectomy is one of the mostly reported and "popular" laparoscopic pancreatic surgical procedures, which may offer many benefits to patients, such as shorter length of hospital stay, fewer complications, and improved quality of life, but the average operative time is up to 10 h. The incidence of POCD after operation is also high (Jacobs and Kamyab, 2013; Mesleh *et al.*, 2013). This may be associated with hypercarbia induced by the long duration of pneumoperitoneum and CO_2 absorption through the peritoneum. Hypercarbia may cause reduction of rSO_2. Another possible reason for causing reduction of rSO_2 is cerebral vasodilation and increased intracranial pressure induced by increased CO_2 (Germon *et al.*, 1995; Konishi and Kikuchi, 1996).

CO_2 is a powerful regulator of cerebrovasculature. Cerebral blood flow will increase or decrease by 2 ml/(100 g·min) correspondingly whenever $PaCO_2$ increases or decreases 0.13 kPa (1 mmHg). Although in normal circumstances, increasing cerebral blood flow will not decrease intracranial pressure and cerebral perfusion with the presence of intracranial compliance, we cannot evaluate whether increasing intracranial pressure and decreasing cerebral blood flow will result in rSO_2 reduction on the basis of expanded cerebrovasculature after inhalational anesthesia.

In a large prospective study (Monk *et al.*, 2002), the incidence of POCD in elderly patients correlated with intra-operative frequently low rSO_2. It is reported that rSO_2 lower than 50% or a decrease in rSO_2 of 20% compared to baseline will prognosticate the possible presence of cerebral ischemia. This conclusion had been proven by the auditory evoked potential test (Blas *et al.*, 1999). Slater *et al.* (2009) also came to a similar conclusion. The patients with rSO_2 score decreasing $\geq 3000\% \cdot s$ in CABG intra-operation would be more likely to develop POCD ($P=0.024$). The risk increases nearly three-fold with prolonged hospital stay.

In our study, the $rSO_{2,\%max}$ in the POCD group was significantly higher than that in the non-POCD group ($P<0.001$). In the non-POCD group, t_1–t_4 rSO_2 values were significantly higher than t_0 rSO_2 value ($P<0.05$). There was no significant difference between rSO_2 values at t_5 and t_0. In the POCD group, rSO_2 at t_1 was significantly higher than that at t_0 ($P<0.05$), while at t_5 it decreased significantly compared with t_0 ($P<0.05$). These data demonstrated that the rSO_2 could correspond to the occurrence of POCD. It was also highlighted that $rSO_{2,\%max}>10.2\%$ was a potential predictor of neurocognitive injury.

Aβ is a polypeptide with a folded configuration and β sheet structure formed by 39–43 amino acids. The molecular weight is about 4 kD. Aβ is an initiating factor of senile plaque formation and the important component of senile plaque nucleus for AD. There is a close relationship between increased Aβ and cognitive dysfunction (Townsend *et al.*, 2002). The increased brain Aβ was related to increased Aβ precursor protein (β-APP) (Grilli *et al.*, 1996). APP is an acute reactive protein that is modulated by central inflammatory cytokines in transcription (Grilli *et al.*, 1996). The generation and accumulated increase of Aβ would further trigger neuronal apoptosis. Aβ can induce NMDA receptors and block transmission of information in neurons, resulting in dysfunction for learning and memory. Sevoflurane can alter the formation of amyloid precursor protein and increase the level of Aβ, which would result in neurotoxicity. Lu *et al.* (2010) also reported that AD transgenic rats are prone to neurologic injury on inhalation of sevoflurane.

Neurodegeneration and anesthesia may be contributing factors to the pathophysiology of POCD (Tang *et al.*, 2010). Inflammation is the bridge between POCD and AD; therefore, surgery and anesthesia may lead to brain inflammation, which may be one of the mechanisms of the increased incidence of POCD (Hu *et al.*, 2010).

Recent studies show that Aβ is one of the potential markers of neurologic damage and persistent inflammation (Gold *et al.*, 2005). Aβ may be associated with increased cognitive dysfunction. A potential relationship between Aβ and POCD may exist and serve as one of the predictors of the increased incidence of POCD and other related biomarkers (Townsend *et al.*, 2002).

Multivariate logistic regression analysis has shown that basal body temperature, $PaCO_2$, $rSO_{2,\%max}$ and Aβ seem to play a more important role for the interpretation of POCD. Routine blood gas analysis, monitoring of rSO_2, and detection of plasma Aβ might be useful tools for predicting the occurrence of POCD. Further studies are required to investigate the importance of plasma Aβ as a potential biomarker for POCD. Findings from the current study may have a significant impact on the promotion and application of laparoscopic pancreaticoduodenectomy and the improvement of prognosis.

Compliance with ethics guidelines

Xi-ming LI, Ming-tao SHAO, Jian-juan WANG, and Yue-lan WANG declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study. Additional informed consent was obtained from all patients for which identifying information is included in this article.

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中文概要：

本文题目：术后认知功能障碍与脑氧饱和度及血浆 β-淀粉样蛋白的关系

Relationship between post-operative cognitive dysfunction and regional cerebral oxygen saturation and β-amyloid protein

研究目的： 探讨腹腔镜胰体尾切除术患者术后认知功能障碍（POCD）的发生与脑氧饱和度（rSO_2）及血浆 β-淀粉样蛋白（Aβ）水平的相关性。

创新要点： POCD 的发生机制与 rSO_2 及 Aβ 有一定的相关性；rSO_2 较基础值下降的最大百分数（$rSO_{2,\%max}$）>10.2%有可能发生 POCD，因此，rSO_2 监测可能是预测 POCD 发生的有效工具；Aβ 可能是发生 POCD 敏感的生化预警指标。

研究方法： 择期行腹腔镜胰十二指肠切除术患者 50 例，于术前 1 天和术后 7 天分别行简明精神状态量表（MMSE）、数字广度、数字符号、循迹连线、词汇流畅性（VFT）和单词辨认神经心理测验。分别于麻醉诱导前（t_0）、气腹开始前（t_1）、气腹 120 min（t_2）、气腹 240 min（t_3）、气腹 480 min（t_4）、气腹结束（t_5）及术毕 24 h，抽取颈内静脉血 3 ml，采用酶联免疫法（ELISA）方法测定 Aβ 含量。术中利用近红外光谱技术（NIRS）连续监测 rSO_2，并计算术中 rSO_2 平均值（$\overline{rSO_2}$）、术中 rSO_2 最小值（$rSO_{2,min}$）和 $rSO_{2,\%max}$。

重要结论： POCD的发生与rSO_2及Aβ有关；危险因素可能有老年、低教育水平、较高基础体温、rSO_2下降、CO_2蓄积、血浆Aβ升高等；rSO_2监测有可能是POCD的有效预测工具之一；Aβ有可能是发生POCD敏感的生化预警标志物之一。

关键词组： 术后认知功能障碍；局部脑氧饱和度；β-淀粉样蛋白