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Effects of pneumoperitoneum and steep Trendelenburg position on cerebral hemodynamics during robotic-assisted laparoscopic radical prostatectomy

A randomized controlled study

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Abstract

Background: We evaluated the relationship between ultrasonographical acquired parameters and short-term postoperative cognitive function in patients undergoing robotic-assisted radical prostatectomy (RALP).

Methods: Ninety elderly patients scheduled for RALP had their optic nerve sheath diameter (ONSD), the cross-sectional area (CSA) of the internal jugular vein (IJV) and the IJV valve (IJVV) competency assessed by ultrasound. The patients were analyzed in 2 groups based on whether displayed IJVV incompetency (IJVVI). The 3 parameters were measured before anesthesia (T0), immediately after induction of general anesthesia (T1), 5 minutes after establishing pneumoperitoneum (T2), 5 minutes after placing the patient in the Trendelenburg position (T3), and 5 minutes after the release of the pneumoperitoneum in the supine position (T4). Regional cerebral tissue oxygen saturation (rSO_2) was also measured by near-infrared spectroscopy intraoperatively. The Mini-Mental State Examination (MMSE) and Confusion Assessment Method (CAM) were performed the day before surgery and on postoperative days 1, 3, and 7.

Results: We found that 52% of patients had evidence of IJVVI after being placed in the Trendelenburg position after pneumoperitoneum was established (T4). Patient with IJVVI showed a significant increase of ONSD and CSA at T1, T2, T3, T4 but there was no associated decrease in rSO_2. MMSE scores were reduced at postoperative day 1 and the 7 patients that developed postoperative delirium came from Group IJVVI.

Conclusions: Our observations suggest that elderly patients that show IJVVI after adequate positioning for RALP may develop elevated intracranial pressure as well as mildly compromised postoperative cognitive function in the short term.

Abbreviations: CAM = Confusion Assessment Method, CSA = cross-sectional area, FiO_2 = inspiration oxygen, ICP = intracranial pressure, IJV = internal jugular vein, IJVV = internal jugular vein valve, IJVVI = internal jugular vein valve incompetency, MMSE = Mini-Mental State Examination, ONSD = optic nerve sheath diameter, POD = postoperative delirium, Pplat = respiratory plateau pressure, RALP = robotic-assisted radical prostatectomy, rSO2 = regional cerebral tissue oxygen saturation.

Keywords: intracranial pressure, postoperative delirium, trenelenburg position

1. Introduction

Robotic assisted laparoscopic surgery is increasingly being performed for range of surgical procedures that were previously amenable only to the open approach. This technique has the benefits of minimizing surgical trauma and postoperative pain, reducing bleeding, and reducing hospital stay.[1–3] Typically, CO_2 pneumoperitoneum and the Trendelenburg position required for such surgery cause significant changes in cerebral hemodynamic physiology and increase intracranial pressure (ICP).[5,6] The optic nerve sheath diameter (ONSD) as determined by noninvasive ocular sonography has been demonstrated as a surrogate measure of elevated intracranial pressure in elderly patients.[7] An increase in ONSD to 6.8 mm is associated to an ICP above 20 mmHg, requiring a change of positioning or a decrease of abdominal pressure.[4] The internal jugular vein valve is the only valve in the pathway of cerebral venous drainage between the thoracic and intracranial cavity and is located at the lower part of internal jugular vein and near the confluence into the brachiocephalic vein. When competent, the valve prevents retrograde venous blood flow back to the brain.[8,9] The IJVVI, is prevalent in patients that are

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old, men and during the Valsalva maneuver[10–12] can interfere with cerebral blood flow autoregulation and elevate ICP. IJVVI, as assessed by ultrasound, was found to be more prevalent in patients with transient global amnesia.[13] Cerebral autoregulation plays a significant role in maintaining constant blood flow and avoiding changes in cerebral perfusion pressure.[14,15] Cerebral autoregulation impairment may relate to unfavorable factors after a neurological event[16,17].

The potential role of IJVVI in the development of postoperative delirium (POD) or postoperative cognitive dysfunction has not been extensively investigated. We hypothesize that IJVVI during robotic assisted laparoscopic prostatectomy maybe associated elevated intracranial pressure and this may have a bearing on postoperative cognitive dysfunction. We aim to demonstrate a relationship between intraoperative IJJVI and ICP and a difference in short term neurological outcome between patients with or without IJVVI as assessed by the Mini-Mental State Examination (MMSE) and the Confusion Assessment Method (CAM).

2. Methods

This study was approved by the University's Institutional Review Board (IRBPJ2016-08-06) and written informed consent was obtained from all subjects participating in the trial. The trial was registered prior to patient enrollment at clinicaltrials.gov (ChiCTR1800015206). We previously performed pilot studies to familiarize ourselves with the techniques of ultrasonographic measurement and neurocognitive evaluation. Ninety adult male patients undergoing RALP that were of American Society of Anesthesiologists physical status class 1 or 2 were initially recruited at the First Affiliated Hospital of Anhui Medical University, Hefei, Anhui. We excluded patients who had previous neurological diseases (history of stroke or transient ischemic attack), mental impairment, visual impairment, drug dependence, and any other comorbidities which preclude neuropsychological testing. After determining the presence or not of IJVVI, the patients were analyzed in 2 groups: those with IJV valve competent (Group IJVVC) and those in whom the IJV valve were incompetent (Group IJVVI). The CONSORT Flow diagram is shown in Fig. 1.

Patients were asked to perform the MMSE on the day before the surgery, postoperative neurocognitive evaluation was performed on postoperative days 1, 3, and 7. All neurocognitive tests were performed by a skilled nurse who has been trained for the task. Postoperative delirium was determined by CAM which included the presence based on 4 features as previously described:

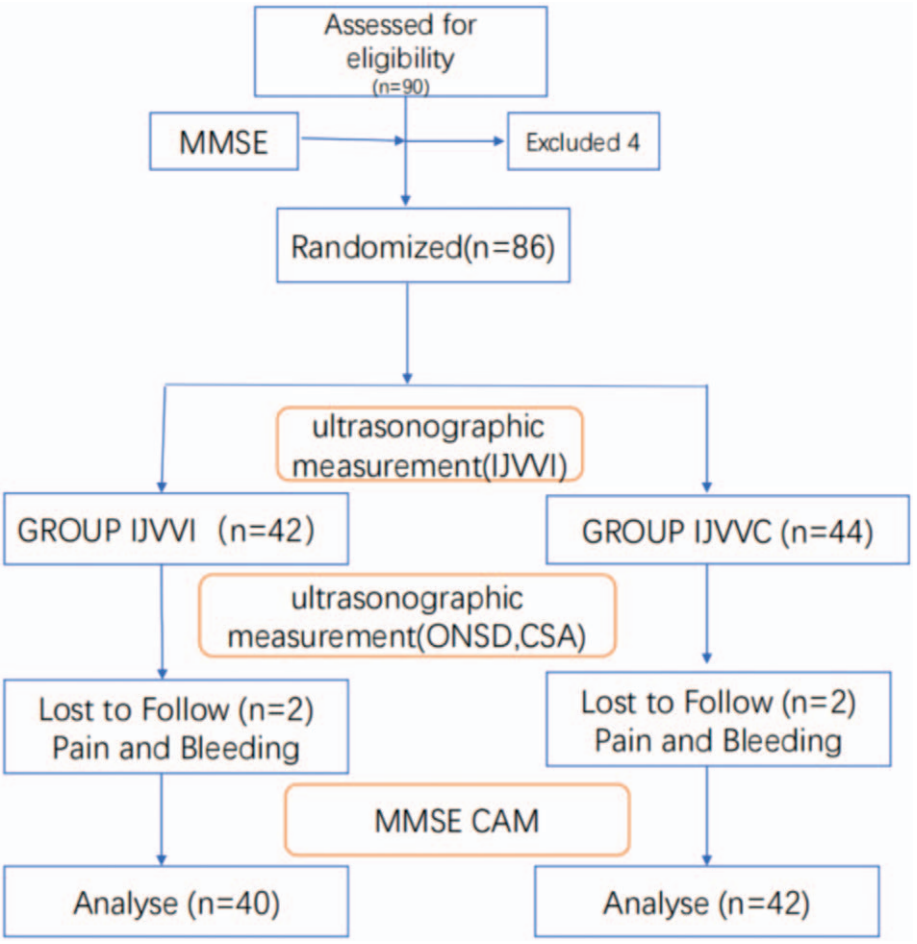

Figure 1. CONSORT flow diagram. All patients were performed MMSE the day before operation. Four of 90 patients were not finished MMSE. The patients were grouped by presence or absence of IJVVI which was considered positive that retrograde flow >0.88 seconds at any side. During the operation, ONSD and CSA were measured by ultrasound. Four patients in groups were lost to follow because of pain and bleeding. MMSE and CAM were diagnosed postoperative cognitive function which was performed by a skilled nurse. CAM = Confusion Assessment Method, CSA = cross-sectional area, MMSE = Mini-Mental State Examination, ONSD = optic nerve sheath diameter.

acute change with a fluctuating course, inattention, disorganized thinking, and altered level of consciousness.[18,19] Data from the MMSE and CAM were reviewed by several other trained individuals not associated with the study to make the final decision.

Standard monitoring including electrocardiography, pulse oximetry, and noninvasive arterial blood pressure was established for the patient upon arrival to the operating room. The values of rSO_2 were monitored with an INVOS 5100B cerebral oximeter (Somanetics, Troy, MI). The sensors were placed bilaterally at least 2 cm above the eyebrow on the right and left sides of the forehead according to the manufacturer's instructions before induction of anesthesia. Measurement of regional cerebral tissue oxygen saturation started before induction of anesthesia and fraction of inspiration oxygen (FiO_2) was maintained at 60% throughout anesthesia. A decrease in cerebral oxygenation of >20% or below the absolute level of 50% was defined as an interventional threshold, resulting in a change of positioning or an increase of FiO_2.

General anesthesia was induced with a bolus dose of propofol 1.5 mg kg^{-1}, sufentanil 0.5 μg kg^{-1}, and cisatracurium 0.15 mg kg^{-1}. The patients' trachea was intubated and mechanical ventilation was instituted with a tidal volume of between 6 and 8 mL kg^{-1}, with the respiratory rate adjusted to maintain an end-tidal carbon dioxide partial pressure of 4.5 to 5.5 kPa during surgery. Anesthesia was maintained with a propofol infusion at 4 to 10 mg kg^{-1} h^{-1}, sevoflurane 0.5 to 1 MAC, cisatracurium 0.05 mg kg^{-1}, and remifentanil 0.25 to 4 μg kg^{-1} min^{-1}. The mean arterial pressure (MAP) was maintained within 20% of baseline in all patients.

Ultrasonographic measurement of ONSD, CSA, and IJVVI were conducted by a single trained investigator who has performed >30 scans prior to the study. The CSA, ONSD was taken an averaged measurement over about 3 times. A 10 MHz linear array transducer was used to examine the IJVVI and CSA (Sonoste, Bothell, WA). A level of 1.5 cm cephalad to the cricoid cartilage, marked for reproducibility, was used as the reference point for the ultrasonic probe placement. The jugular blood flow direction at the head of the valves was evaluated with color and pulsed wave Doppler. The presence of IJVVI was defined as continuous retrograde flow >0.88 seconds on any side.[20] The CSA was imaged 2 cm below the carotid bifurcation with care taken not to compress the vein. The ONSD was measured at a point 3 mm behind the optic disc.[21] Each optic nerve in the transverse plane and in the sagittal plane was measured 2 times. The final ONSD corresponded to the average of the 8 values measured in both eyes of each patient.

Measurements were made at 5 distinct time points: at baseline before induction of anesthesia in the supine position (T0), 5 minutes after induction of anesthesia in the supine position (T1), 5 minutes after onset of pneumoperitoneum at a target abdominal pressure of 15 mmHg (T2), 5 minutes after placing the patient in the steep Trendelenburg position (T3), and 5 minutes after returning to the supine position at the end of surgery (T4).

Statistical analysis was performed using SPSS version 18.0 (SPSS Inc., Chicago, IL). Based on a pilot study, we calculated that a sample size of 23 subjects would be required with an alpha of 0.05 and a power of 90%. With an anticipated 10% loss to follow-up, we set our sample size at 60 patients for our primary outcome. Data are described as mean ± standard deviation. Demographic variables, blood loss, urine output, and intravenous fluid volume between groups were compared using unpaired Student *t* tests. A 2-way repeated-measures analysis of variance (ANOVA) with post hoc unpaired *t* test and Bonferroni correction was used to compare rSO_2, MAP, HR, Pplat, ONSD, and CSA between the groups. A one-way repeated-measures ANOVA with Bonferroni post hoc tests were used to analyze these variables across time within the groups. All statistical tests were 2-tailed. A *P* value <.05 was considered as statistically significant.

3. Results

A total of 90 patients were assessed for eligibility. Then, 4 patients did not pass the MMSE test, and 4 patients lost to follow up in this study because of postoperative pain and bleeding. Therefore, 82 patients completed this study. The patient and intraoperative characteristics are shown in Table 1.

Sonography identified IJVVI at T2 or T3 in 40 patients with the other 42 assigned to the IJVVC group. The mean values of ONSD and CSA at T3 significantly increased compared with that at T0 for each group. In the IJVVI group, the mean value of ONSD and CSA at T3 increased significantly compared with the IJVVC group. Although we changed the position decrease the abdominal pressure, the ONSD of 1 patient increased to 7.4 mm at T3 in the IJVVI group. (Fig. 2A and B).

MMSE was performed the day before surgery, the score was not significant between 2 groups. MMSE score had statistically significant decrease in the group compared with the IJVVC group on postoperative day 1 but did not remain so on days 3 and 7 postsurgery (Fig. 3). There was evidence for postoperative delirium in 7 patients in the IJVVI group compared with 1 patient from the IJVVC group on day 1. This number dropped to 1 and 0, respectively, on days 3 and 7. The intraoperative values for rSO_2 in 2 groups did not change significantly between the various timepoints (Table 2).

4. Discussion

While undoubtedly there are major advantages associated with laparoscopic approach for major surgery, it does necessitate the patients being placed in a steep head-down position for several hours and subjected to CO_2 pneumoperitoneum. The combine effect of both these measures can cause significant perturbations in different bodily systems such as increased intracranial and intraocular pressures, reduced venous return from and increased central venous pressure, reduced functional residual capacity and increased intrathoracic pressure, with their function being

Table 1

Patient characteristics, duration of surgery, blood loss, fluid administration, and urine output in patients.

Characteristic	Group IJJVI	Group IJJVC	*P*
Age, y	65.1 ± 4.0	65.2 ± 3.8	.21
Weight, kg	65.8 ± 6.2	65.9 ± 4.9	.65
Height, cm	164.4 ± 7.1	166.3 ± 4.1	.22
Anesthetic time, min	305.7 ± 25.8	306.4 ± 15.1	.69
Operation time, min	250.2 ± 23.1	249.5 ± 15.2	.73
Fluid administered, mL	1533.0 ± 126.0	1412.0 ± 86.8	.78
Blood loss, mL	117.1 ± 9.1	124.6 ± 20.0	.12
Urine output, mL	160.0 ± 29.5	157.0 ± 24.0	.15

Data are expressed as mean ± SD, there were no statistically significant differences between the 2 groups. IJJVC = internal jugular vein valve competent, IJJVI = internal jugular vein valve incompetency.

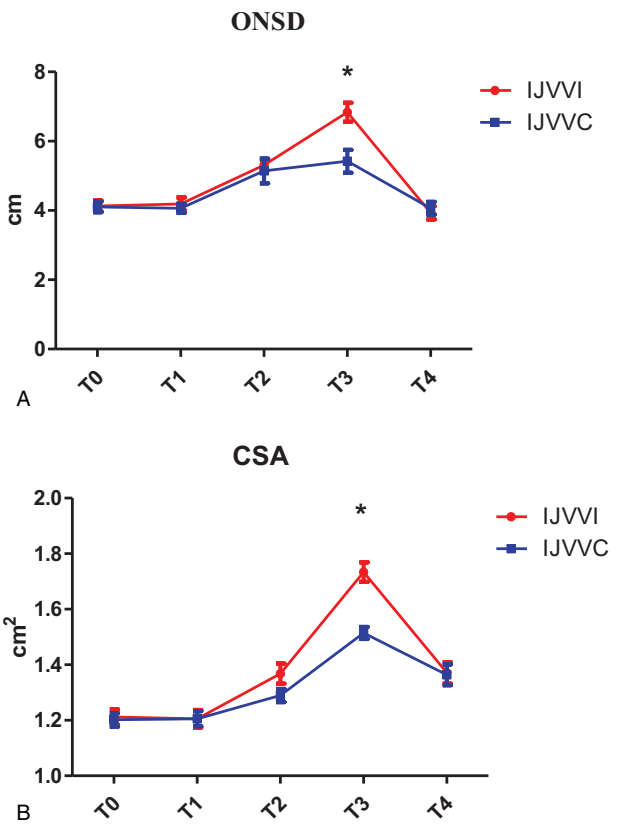

Figure 2. A, ONSD means and standard deviation, in different time. B, CSA means and standard deviation, in different time. $^{*}P < .05$ significantly different from Group IJVVC. T0, before anesthesia; T1, immediately after induction of general anesthesia; T2, in the supine position after pneumoperitoneum insufflation; T3, after Trendelenburg positioning; and T4, again at the end of the procedure. CSA = cross-sectional area, ONSD = optic nerve sheath diameter.

compromised.[22–24] Using ultrasound to assess surrogate measures of raised intracranial pressure, namely optic nerve diameter and the cross-sectional area of the internal jugular vein, we were able to differentiate those who may experience more severe pressure increases based on whether they have demonstrable internal jugular vein valve incompetency. Interestingly,

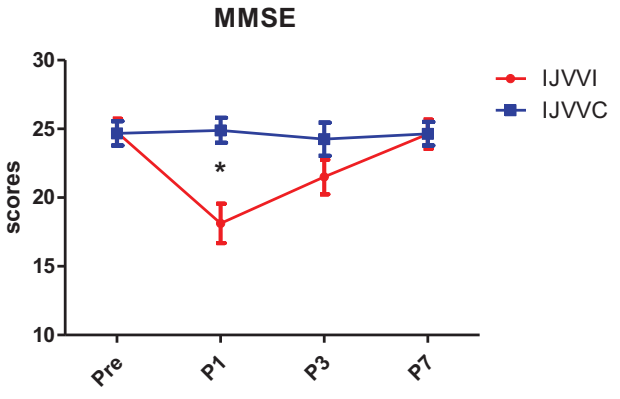

Figure 3. MMSE scores were measured at preoperation and postoperation 1, 3, 7 days; $^{*}P < .05$ significantly different from Group IJVVC. MMSE = Mini-Mental State Examination, P1 = postoperation day 1, P3 = postoperation day 3, P7 = postoperation day 7, Pre = preoperation.

there were no difference in cerebral oxygen saturation between the groups but those with valve incompetence may be more prone to develop delirium as well as short-term cognitive changes postoperatively.

In this study, optic nerve diameter ultrasonography as a surrogate measure for intracranial pressure was adopted, because it is a noninvasive and reproducible technique for the assessment of ICP and can be readily performed in patients undergoing laparoscopic abdominal and pelvic surgery. Several studies have demonstrated good correlation between optic nerve diameter ultrasonography and invasive ICP measurements,[21] with favorable specificity and sensitivity.[25] As a result, monitoring the ONSD could afford useful information for changes in ICP intraoperatively. For those with IJV valve incompetency, we found the ONSD increased from 4.3 to 6.8 mm when they were placed in steep Trendelenburg position and pneumoperitoneum but not in those whose valve is competent. The subarachnoid space surrounding the retrobulbar portion of the optic nerve in these cases was distensible and expanded as cerebrospinal pressure increases. Some studies proposed that inverted fluid shift and venous engorgement due to the Trendelenburg position, as well as the impediment of cerebral venous drainage were the major factor that leading to such increases in ICP.[15] These propositions are in agreement with our findings, especially under general anesthesia where the ICP may raise more rapidly.[26]

The Valsvalva Maneuver, application of PEEP, and changes in body position has been shown to increase CSA,[31] which may cause the incidence of IJVVI. In the IJVVI group, there were more significantly increases the CSA of the IJV when patients were placed in Trendelenburg positioning, compared with the patients in the IJVVC group. It is interesting to note that the Trendelenburg position does not alter the CSA in a predictable way.

In our study, we found 28 IJVVI patients after TP or PP that may endure small transvalvular pressure gradient in supine position, could come out by reduced intrathoracic pressure when the transvalvular pressure gradient increases more than abnormal valves can bear. The Trendelenburg position may lead to higher intrathoracic pressure when the same tidal volume used for the supine position in order to maintain $PaCO_2$. Therefore, IJVVI may disturb cerebral venous drainage because of the increased impedance of the lungs to inflation and the increased intrathoracic pressure.[27]

In theory, patients with IJVVI may have a greater risk of cerebral hypoperfusion from raised intracranial pressure than patients without IJVVI steep Trendelenburg position for hours, which might result in ischemia to the brain. Transient cerebral ischemia may not result in permanent deficits. Our cohort of patients as a whole did not demonstrate any substantial reduction in cerebral oxygenation and but those with IJVVI. However, the MMSE scores of those with IJVVI was less than those patients with competent valves on day 1 post op but recovered on days 3 to 7, indicating a short-term effect. A study also found that IJJVI resulted in a lower MMSE score on postoperative day without any other significant differences in a battery of neurocognitive assessments.[11]

Postoperative delirium is a common postoperative complication in elderly patients, with a 15% to 25% incidence after major surgery, most often diagnosed using CAM, and requires a careful evaluation for and the treatment of reversible causes.[28] Although the availability of epidemiological data regarding delirium continues to grow, knowledge regarding its

Table 2

Perioperative hemodynamics, ventilation, and cerebral oxygenation during operation.

	T0	T1	T2	T3	T4
MAP, mmHg					
Group IJVVI	88.00 ± 4.46	82.81 ± 6.83	91.12 ± 8.76	93.4 ± 6.32	85.69 ± 7.14
Group IJVVD	89.43 ± 3.17	84.03 ± 6.73	88.15 ± 7.76	92.2 ± 8.58	87.18 ± 7.46
P	.101	.419	.109	.473	.360
HR, bpm					
Group IJVVI	68.48 ± 8.59	65.14 ± 6.40	64.71 ± 6.18	70.4 ± 2.64	68.9 ± 3.59
Group IJVVD	67.18 ± 6.86	64.3 ± 5.79	65.68 ± 6.66	69.85 ± 5.83	67.7 ± 6.03
P	.450	.534	.500	.584	.279
Pplat, mmHg					
Group IJVVI		17.03 ± 2.40	22.49 ± 1.18	26.67 ± 1.74	19.16 ± 1.44
Group IJVVD		16.22 ± 2.25	21.98 ± 1.95	27.18 ± 0.62	18.58 ± 1.97
P		.121	.159	.082	.130
rSO_2 (%)					
Group IJVVI	72.64 ± 3.27	72.95 ± 4.06	70.76 ± 1.41	69.93 ± 2.21	73.14 ± 2.76
Group IJVVD	72.23 ± 3.21	72.25 ± 3.39	71.23 ± 3.41	70.13 ± 2.54	72.20 ± 3.20
P	.562	.399	.430	.709	.156

Values are the mean ± SD. HR = heart rate, IJJVC = internal jugular vein valve competent, IJJVI = internal jugular vein valve incompetency, MAP = mean arterial blood pressure, Pplat = respiratory plateau pressure, rSO_2 = regional cerebral oxygen saturation. T0 = before anesthesia, T1 = immediately after induction of general anesthesia, T2 = in the supine position after pneumoperitoneum insufflation, T3 = after Trendelenburgpositioning; T4 = again at the end of the procedure. There were no statistically significant differences between the 2 groups.

pathophysiology and therapy is less well understood. Interestingly there were more patients with IJVVI that showed symptoms of delirium on postoperative day 1 but as our study was not powered for that, further work is warranted.

It is accepted by some that rSO_2 reflects the regional balance between cerebral tissue oxygen supply and demand, and this parameter has been examined to determine the effects of various positions on cerebral blood flow under a range of positions during robot assisted laparoscopic surgery.[29] Consistent with a previous study,[30] we found that the rSO_2 showed no significant changes at all the predetermined time points in the course of surgery.

The major limitation with the present study is the intermittent nature of our measurements. Although we marked the location for ultrasound probe placement there could still be a degree of operator dependency in the readings. As the primary aim of the study is to evaluate whether we can demonstrate an increase in ICP based on IJVVC, we only used the MMSE to assess for postoperative cognitive dysfunction whereas a more detailed battery of tests may reveal more subtle differences in cognition.

5. Conclusions

Intraoperative ultrasonographic assessment of IJVV competency maybe a useful approach of stratifying those patients who may develop increased intracranial pressure. There may be a potential link between prolonged increase in ICP from steep Trendelenburg positioning and pneumoperitoneum and short term postoperative cognitive impairment but larger studies using more detailed neurocognitive testing is required to confirm this relationship.

Author contributions

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Critical revision of the article and obtaining funding: Xuesheng Liu, Yao Lu, Yuanhai Li, and Gordon Tin Chun Wong.
Data collection: Ke Chen and Qing Wang.
Data curation: Qing Wang, Yao Lu.
Writing – original draft: Ke Chen, Lizhen Wang.
Writing – review & editing: Xuesheng Liu, Yuanhai Li, Gordon Tin Chun Wong.
Writing the article: Ke Chen, Lizhen Wang, Yao Lu, and Gordon Tin Chun Wong.

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