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 (IJVVVI). 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 (rSO2) 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 IJVVVI after being placed in the Trendelenburg position after pneumoperitoneum was established (T4). Patient with IJVVVI showed a significant increase of ONSD and CSA at T1, T2, T3, T4 but there was no associated decrease in rSO2. MMSE scores were reduced at postoperative day 1 and the 7 patients that developed postoperative delirium came from Group IJVVVI.

Conclusions: Our observations suggest that elderly patients that show IJVVVI 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, FiO2 = inspiration oxygen, ICP = intracranial pressure, UV = internal jugular vein, UVV = internal jugular vein valve, UIVI = 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, treneelenburg 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. Typically, CO2 pneumoperitoneum and the Trendelenburg position required for such surgery cause significant changes in cerebral hemodynamic physiology and increase intracranial pressure (ICP). The optic nerve sheath diameter (ONSD) as determined by noninvasive oculic sonography has been demonstrated as a surrogate measure of elevated intracranial pressure in elderly patients. An increase in ONSD to 6.8mm is associated to an ICP above 20mmHg, requiring a change of positioning or a decrease of abdominal pressure. The internal jugular vein valve is the only valve in the path 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. The IJVVVI, is prevalent in patients that are...
old, men and during the Valsalva maneuver\textsuperscript{[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.\textsuperscript{[13]} Cerebral autoregulation plays a significant role in maintaining constant blood flow and avoiding changes in cerebral perfusion pressure.\textsuperscript{[14,15]} Cerebral autoregulation impairment may relate to unfavorable factors after a neurological event\textsuperscript{[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 IJVVI 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](https://example.com/figure1.png)

**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. \cite{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 oximetry \cite{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 in 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 was 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. \cite{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. \cite{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 combined 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. IJVVC = internal jugular vein valve competent, IJVVI = internal jugular vein valve incompetence.
strable internal jugular vein valve incompetency. Interestingly, severe pressure increases based on whether they have demonstrable internal jugular vein valve incompetency. [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, 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.[16]

The Valsalva 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 IJVVI 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 PaCO2. 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 IJVVI resulted in a lower MMSE score on postoperative day without any other significant differences in a battery of neurocognitive assessments.[31]

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

![Figure 2](image-url)  
**Figure 2.** A. ONSD means and standard deviation, in different time. B, CSA means and standard deviation, in different time. 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.

![Figure 3](image-url)  
**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.
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 rSO2 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.[30] Consistent with a previous study, we found that the rSO2 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 of 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 may be 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.

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Reference
[1] Mahida JB, Asti L, Deans KJ, et al. Laparoscopic pyloromyotomy decreases postoperative length of stay in children with hypertrophic pyloric stenosis. J Pediatr Surg 2016;51:1436–9.
[2] Closhen D, Treiber AH, Berres M, et al. Robotic assisted.prostactic surgery in the Trendelenburg position does not impair cerebral oxygenation measured using two different monitors: a clinical observational study. Eur J Anaesthesiol 2014;31:104–9.
[3] Neira VM, Kovess T, Guerra L, et al. The impact of pneumoperitoneum and Trendelenburg positioning on respiratory system mechanics during laparoscopic pelvic surgery in children: a prospective observational study. Can J Anaesth 2015;62:798–806.
[4] Robba C, Bacigaluppi S, Cardim D, et al. Intraoperative non-invasive intracranial pressure monitoring during pneumoperitoneum: a case report and a review of the published cases and case report series. J Clin Monit Comput 2016;30:527–38.
[5] Ozcan MF, Akbulut Z, Gurdal C, et al. Does steep Trendelenburg positioning effect the ocular hemodynamics and intraocular pressure in patients undergoing robotic cystectomy and robotic prostatectomy? Int Urol Nephrol 2017;49:55–60.
[6] Ozcan MF, Akbulut Z, Gurdal C, et al. Time course of cerebrovascular autoregulation during extreme Trendelenburg position for robotic-assisted prostactic surgery. Anaesthesia 2014;69:58–63.
[7] Chin JH, Seo H, Lee EH, et al. Sonographic optic nerve sheath diameter as a surrogate measure for intracranial pressure in anesthetized patients in the Trendelenburg position. BMC Anesthesiol 2015;15:43.
[8] Liu H, Cao X, Zhang M, et al. A case report of cough headache with transient elevation of intracranial pressure and bilateral internal jugular vein valve incompetence: a primary or secondary headache? Cephalalgia 2018;38:600–1.
[9] Dopp F, Valduze JM, Schreiber SJ. Incompetence of internal jugular valve in patients with primary exertional headache: a risk factor? Cephalalgia 2008;28:182–5.
[10] Styczinsky G, Dobosiewicz A, Abramczyk P, et al. Internal jugular vein valve insufficiency in cough syncope. Neurology 2008;70:812–3.
[11] Roh GU, Kim WO, Rha KH, et al. Prevalence and impact of incompetence of internal jugular valve on postoperative cognitive dysfunction in elderly patients undergoing robot-assisted laparoscopic radical prostatectomy. Arch Gerontol Geriatr 2016;64:167–71.

Table 2
Perioperative hemodynamics, ventilation, and cerebral oxygenation during operation.

|            | T0          | T1          | T2          | T3          | T4          |
|------------|-------------|-------------|-------------|-------------|-------------|
| MAP, mmHg  |             |             |             |             |             |
| Group LVI  | 88.00±4.46  | 82.81±6.83  | 91.12±8.76  | 93.4±6.32   | 85.69±7.14  |
| Group LVVD | 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 LVI  | 68.48±8.59  | 65.14±6.40  | 64.71±6.18  | 70.4±2.64   | 68.9±3.59   |
| Group LVVD | 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 LVI  | 17.03±2.40  | 22.49±1.18  | 26.67±1.74  | 19.16±1.44  |             |
| Group LVVD | 16.22±2.25  | 21.98±1.95  | 27.18±0.62  | 18.58±1.97  |             |
| P          | .121        | .159        | .082        | .130        |             |
| rSO2 (%)   |             |             |             |             |             |
| Group LVI  | 72.64±3.27  | 72.95±4.06  | 70.76±1.41  | 69.93±2.21  | 73.14±2.76  |
| Group LVVD | 72.23±3.21  | 72.25±3.39  | 71.23±3.41  | 70.13±2.54  | 72.20±3.20  |
| P          | .362        | .399        | .430        | .709        | .156        |

Values are the mean±SD. HR=heart rate, IJV=internal jugular vein valve competent, IJV=internal jugular vein valve incompetence, MAP=mean arterial blood pressure, Pplat=respiratory plateau pressure, rSO2=regional cerebral oxygen saturation. T0=before anesthesia, T1=immediately after induction of general anesthesia, T2=in the supine position after pneumoperitoneum insufflation, T3=after Trendelenburg positioning, T4=again at the end of the procedure. There were no statistically significant differences between the 2 groups.

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[12] Hansrami V, Dhorat Z, McCollum CN. Diagnosing of pelvic vein incompetence using minimally invasive ultrasound techniques. Vascular 2017;25:253–9.

[13] Cejas C, Csisneros LF, Lagos R, et al. Internal jugular vein valve incompetence is highly prevalent in transient global amnesia. Stroke 2010;41:67–71.

[14] Doc A, Kumagai M, Tamura Y, et al. A comparative analysis of the effects of sevoflurane and propofol on cerebral oxygenation during steep Trendelenburg position and pneumoperitoneum for robotic-assisted laparoscopic prostatectomy. J Anesth 2016;30:949–55.

[15] Kalmar AF, Foubert L, Hendrickx JFA, et al. Influence of steep Trendelenburg position and CO2 pneumoperitoneum on cardiovascular, cerebrovascular, and respiratory homeostasis during robotic prostatectomy. Br J Anesth 2010;104:433–9.

[16] Hovens IB, van Leeuwen BL, Mariani MA, et al. Postoperative cognitive dysfunction and neuroinflammation; cardiac surgery and abdominal surgery are not the same. Brain Behav Immun 2016;54:178–93.

[17] Jantzie LL, Corbett CJ, Berglass J, et al. Complex pattern of interaction between in utero hypoxia-ischemia and intra-amniotic inflammation disrupts brain development and motor function. J Neuroinflammation 2014;11:131.

[18] Inouye SK, van Dyck CH, Alexi CA, et al. Clarifying confusion: the confusion assessment method: a new method for detection of delirium. Ann Intern Med 1990;113:941–8.

[19] Saczynski JS, Marcantonio ER, Quach L, et al. Cognitive trajectories after postoperative delirium. N Engl J Med 2012;367:30–9.

[20] Nedelmann M, Teschner D, Dieterich M. Analysis of internal jugular vein insufficiency-a comparison of two ultrasound methods. Ultrasound Med Biol 2007;33:857–62.

[21] Kim MS, Bai SJ, Lee JR, et al. Increase in intracranial pressure during carbon dioxide pneumoperitoneum with steep Trendelenburg positioning proven by ultrasonographic measurement of optic nerve sheath diameter. J Endourol 2014;28:801–6.

[22] Kadono Y, Yaegashi H, Machioka K, et al. Cardiovascular and respiratory effects of the degree of head-down angle during robot-assisted laparoscopic radical prostatectomy. Int J Med Robot 2013;9:17–22.

[23] Lestar M, Gunnarsson L, Lagerstrand L, et al. Hemodynamic perturbations during robot-assisted laparoscopic radical prostatectomy in 45° Trendelenburg position. Anesth Analg 2011;113:1069–73.

[24] Kilic OF, Börgers A, Köhne W, et al. Effects of steep Trendelenburg position for robotic-assisted prostatectomies on intra- and extrathoracic air ways in patients with or without chronic obstructive pulmonary disease. Br J Anaesth 2015;114:70–6.

[25] Yoo YC, Kim NY, Shin S, et al. The intraocular pressure under deep versus moderate neuromuscular blockade during low-pressure robot assisted laparoscopic radical prostatectomy in a randomized trial. PLoS One 2015;10:e0135412.

[26] Geeraerts T, Merceron S, Benhamou D, et al. Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. Intensive Care Med 2008;34:2062–7.

[27] Jo YY, Kim JY, Chang YJ, et al. The effect of equal ratio ventilation on oxygenation respiratory mechanics, and cerebral perfusion pressure during laparoscopy in the trendelenburg position. Surg Laparosc Endosc Percutan Tech 2016;26:221–5.

[28] Edward R, Marcantonio. Delirium in hospitalized older adults. N Engl J Med 2017;377:1456–66.

[29] Park EY, Koo BN, Min KT, et al. The effect of pneumoperitoneum in the steep Trendelenburg position on cerebral oxygenation. Acta Anaesthesiol Scand 2009;53:895–9.

[30] Closhen D, Treiber AH, Berres M, et al. Robotic assisted prostatic surgery in the Trendelenburg position does not impair cerebral oxygenation measured using two different monitors. Eur J Anaesthesiol 2014;31:104–9.

[31] Nassar B, Deol GRS, Ashby A, et al. Trendelenburg position does not increase cross-sectional area of the internal jugular vein predictably. Chest 2013;144:177–82.