Randomized Controlled Trial

# The Effect of Normal Saline Injection Volumes on the Optic Nerve Sheath Diameter during Thoracic Epidural Analgesia

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**Background:** Saline or local anesthetic injection into the epidural space increases intracranial pressure (ICP), at least transiently. Measurement of the optic nerve sheath diameter (ONSD) using ocular ultrasonography is one of the noninvasive methods for ICP assessment.

**Objectives:** The purpose of this study is to investigate the effects of the different volume on the ONSD and cerebral oxygen saturation ($rSO_2$) during thoracic epidural saline injection under awake conditions.

**Study Design:** Prospective randomized, controlled trial.

**Setting:** An interventional pain management practice in South Korea.

**Methods:** This study included 71 patients receiving thoracic epidural catheterization for pain management, following upper abdominal or thoracic surgery. Following successful epidural space confirmation, patients were randomly allocated to receive 5 mL (5 mL group), 10 mL (10 mL group), and 20 mL (20 mL group) of epidural normal saline. Transorbital sonography was performed to measure the ONSD. This was measured at 3 mm posterior to the optic nerve head. An $rSO_2$ was measured using cerebral oximeter sensors.

**Results:** All 3 groups showed significant increases of ONSD from 10 minutes to 40 minutes as compared to baseline (before procedure). Among the 3 groups, the 20 mL group demonstrated the most significantly increased ONSD, as compared to the 5 mL and 10 mL groups. At the 20 minute and 40 minute time points, the ONSD showed a volume-dependent increase ($P = 0.0005$, $P = 0.014$). All 3 groups showed the $rSO_2$ to be distributed between 60~70% without any statistical difference.

**Limitations:** We could not determine the returning point of the normalized ONSD value.

**Conclusion:** Twenty milliliters of normal saline epidural injection resulted in a significant increase of ONSD, as compared to the 5 mL and 10 mL groups. Our results also indicate that an increase of ONSD occurs in accordance with the injected volume of normal saline.

**Key words:** Cerebral oxygen saturation epidural, optic nerve sheath diameter, volume

**Trial registry number:** Clinical trial registry information service (NCT04412109).

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Thoracic epidural analgesia is the gold standard technique for postoperative pain control following major thoracic and upper abdominal surgery, due to its satisfactory results (1-3).

Previous studies have demonstrated that a high injection volume during thoracic epidural anesthesia (TEA) results in a significant increase in thoracic sensory blockade and epidural distribution (4). The effect of different injection volumes has also been demonstrated by the study of thoracic epidurography using different

volumes of contrast medium (5). If the main purpose of thoracic epidural analgesia is for relief of postoperative pain, the injection volume rarely exceeds 5 mL in most of cases. However, many physicians prefer combining TEA with general anesthesia for the purpose of intraoperative pain control (6,7). Although the optimal injection volume for TEA when combined with general anesthesia varies depending on the concentration of local anesthetics, age, height, and type of surgery, the epidural injection volume can be increased, compared to the injection volume of postoperative pain control (6-8).

Epidural injection increases intracranial pressure (ICP) at least transiently (9-11). Moreover, if the injection volume becomes higher, it affects ICP significantly. Previous study showed that higher volumes of local anesthetics reduced cerebral blood flow and regional oxygenation by increasing ICP in infants (12). Similar results to this study were found as increased intracranial pressure by injection of higher volume during caudal block has been reported (9). Hence, using a high volume of local anesthetics during TEA warrants a careful consideration.

Direct measurement of ICP requires measuring pressure in the ventricle or the brain parenchyma (13). Because such techniques as ICP measurement are invasive, optic nerve sheath diameter (ONSD) measurement by ocular ultrasonography has been advocated as a non-invasive tool. Numerous studies have proven that ONSD measured by ocular ultrasound correlates well with the degree of ICP changes (13-18). This measurement technique has also shown excellent intra-observer and inter-observer reproducibility (0.25 ~ 0.3 mm) (9,19,20).

We hypothesized that using a higher volume of normal saline can affect the increase of ONSD during TEA.

The primary endpoint of this study is to compare the values of ONSD measured by ocular ultrasonography and regional cerebral oxygenation ($rSO_2$) in 3 groups receiving different injection volumes during TEA.

## Methods

### Patients

This prospective and randomized study was approved by the Institutional Review Board (IRB #01-081-003) of our institution. The potential benefits and risks of this study were fully explained before patient enrollment and patients were provided informed consent. We registered this study before patient enrollment at clinical trials.gov (NCT04412109, Date of registration: 28th-May-2020).

Inclusion criteria were: 1) patients undergoing hepatobiliary, pancreatic, lung, or gastric surgery due to cancer, and 2) abdominal aortic aneurysm repair patients, who were scheduled to receive thoracic epidural catheterization for postoperative pain control. Ten patients refused to participate in this study. Therefore, the final number of patients included in the study was 71. _Patients were between 36 to 81 years of age (May ~ November, 2020). We excluded patients with coagulopathy, infection, previous history of brain surgery, cerebrovascular disease, or ophthalmic disease.

### Procedure of Thoracic Epidural Catheter Insertion

A fully trained pain physician with various experiences in fluoroscopic guided intervention performed all thoracic epidural catheterization. The patient's upper back was sterilized using a povidone-iodine solution. Using paramedian approach, a 17 gauge Tuohy needle was directed slowly, targeting the interlaminar space of ninth to tenth thoracic vertebra. When the Touhy needle finally came closer than the expected spinolaminar line in a lateral view, epidural space was verified using a loss of resistance with air. Final thoracic epidural space was verified in the anteroposterior (AP) and lateral views using 2 mL of contrast medium. After successful confirmation of epidural space, an epidural catheter was slowly inserted through the Touhy needle and advanced until seventh to eighth thoracic vertebrae. The catheter was fixed firmly with an adhesive plaster.

### Group Allocation

We focused on measuring the ONSD using ultrasonography with 3 different injection volumes. Therefore, patients were randomly assigned to be in 1 of 3 groups receiving different injection volumes. The 3 groups were patients receiving 5 mL (5 mL group), 10 mL (10 mL group) or 20 mL (20 mL group) of 0.9% normal saline, determined by a computer-generated randomization table. Once a successful epidural injection was verified, normal saline was injected through an epidural catheter, according to the assigned group.

### Measurement of ONSD

A single trained investigator, who had done more

than 200 cases of ONSD measurement and had experience with previous studies (11,21,22) conducted this ultrasonographic measurement. This investigator was blinded to the group assignment.

Transorbital sonography using a hockey-stick probe (GE Healthcare, Logiq S8, Milwaukee, USA) was performed to measure ONSD. The power output was reduced (mechanical index, 0.2; thermal index, 0) to minimize the risk of ultrasound-induced eye injury. Patients were asked to close their eyes and a sterile gel was applied on each closed upper eyelid. The hockey stick probe was placed gently to minimize the pressure exerted on the eyeball. After placing the probe on the upper eyelid, it was tilted from anterior to posterior direction to obtain the best axial image of the orbit in the plane of the optic nerve. Axial image of orbit was obtained with the depth of 3.0-4.0 cm. ONSD was measured 3 mm posterior to the optic nerve head (Fig. 1) (9,11,23). ONSD images were captured with no further external stimuli.

Each ONSD was measured serially in each eye at the following time points: before (baseline, T0), 10 minutes (T10), 20 minutes (T20), and 40 minutes (T40) following injection of 5 mL, 10 mL or 20 mL of normal saline according to assigned group.

This measurement was performed twice at each time point, on both the right and left side to obtain more reliable ONSD value. The four measurements' mean values were considered to be the ONSD at each time point. If the measured ONSD was more than 5.5 mm, which was the cut-off point in the previous study, such patients were considered to have increased ICP (16).

After finishing the ONSD measurement, presence of possible complications of increased ICP, such as blurred vision, dizziness, nausea, vomiting, and headache were checked.

### Measurement of $rSO_2$

An $rSO_2$ was assessed from T0 to T40. Cerebral oximeter sensors were applied 2 cm above the eyebrow, on the left and right sides of the forehead bilaterally, prior to TEA. The $rSO_2$ values were continuously monitored using O3 regional oximetry (Root®, Masimo Corp, Irvine, CA, USA).

### Statistical Analysis

This study was focused on evaluating whether there would be any differences in ONSD according to different normal saline injection volume. Previous studies demonstrated that a difference in ONSD > 0.5 mm (10% of mean ONSD in asymptomatic normal adults [mean ONSD 4.9 mm]) would be clinically relevant (16). Twenty patients were required in each group using a two-sided t-test, a significance level of 5%, a power of 80%, and a dropout rate of 15%.

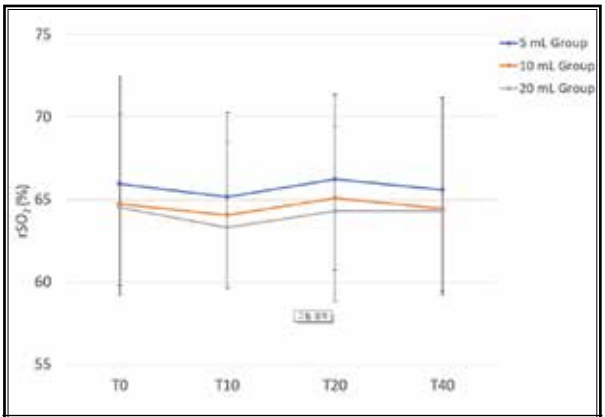


Fig. 1. *Optic nerve sheath diameter (ONSD) measurement by ultrasonography. ONSD was measured 3 mm posterior to the optic nerve head (A-B) in the axial image of the obit in the plane of optic nerve.*

Continuous variables are presented as mean ± standard deviation or median (interquartile range). Categorical variables are presented as number (percentile). Demographic data was compared by unpaired t-test, chi square test, or Fisher's exact test. Repeated ONSD measurements were performed to evaluate the differences between the 3 groups with repeated measures of ANOVA. Intergroup comparison of the changes in ONSD over time was performed through group-by-time interaction. Post hoc analyses for ONSD with Bonferroni correction were performed. All statistical values were two-tailed and *P*-values < 0.05 were considered to be statistically significant. Statistical evaluations were performed using SPSS v 22.0 (IBM, NY, USA).

## Results

Eligibility was assessed in 78 patients and 71 of these patients completed this study (May ~ November, 2020) without dropouts (Fig. 2). Demographic data for thoracic epidural catheterization showed male predominance in 10 mL and 20 mL groups, compared to 5 mL group. Surgeries for lung or liver lobectomy, laparoscopic gastrectomy, Whipple's operation, donor surgery for liver transplantation, and abdominal aortic aneurysm were included (Table 1).

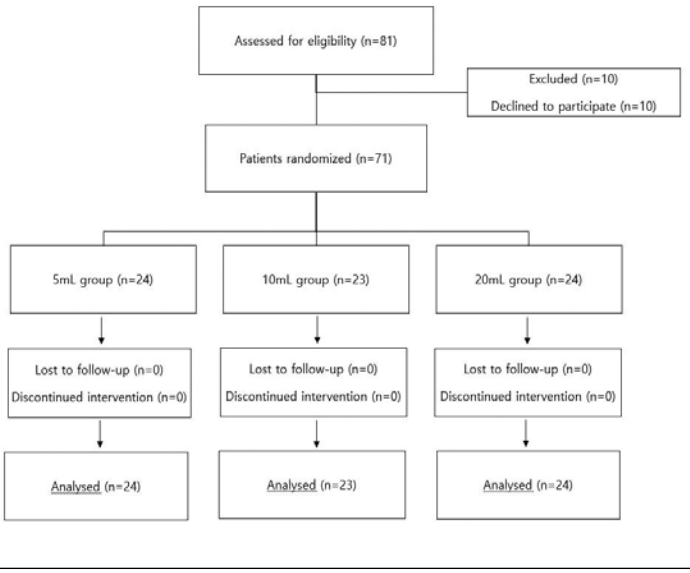


Fig. 2. *Flow chart showing patients who participated in this study.*

Table 1. *Demographic data and type of disease required for thoracic epidural catheterization*

| | 5 mL Group (n = 24) | 10 mL Group (n = 23) | 20 mL Group (n = 24) | *P* value |
|---|---|---|---|---|
| Gender (male/female) | 12 (50)/12 (50) | 17 (73.9)/6 (26.1) | 21(87.5).3 (7.1) | 0.016 |
| Age (years) | 58.5 ± 11.7 | 60.1 ± 11.1 | 62.8 ± 9.2 | 0.364 |
| Body mass index (kg/m$^2$) | 26.2 ± 3.8 | 24.3 ± 4.8 | 24.1 ± 3.9 | 0.052 |
| Type of Disease | | | | 0.421 |
| Gastric cancer | 11 (45.8) | 12 (52.2) | 10 (41.7) | |
| Lung cancer | 6 (25.0) | 4 (17.4) | 5 (20.8) | |
| Hepatobiliary cancer | 1 (4.2) | 5 (21.7) | 7 (29.2) | |
| Pancreas cancer | 1 (4.2) | 1 (4.3) | 1 (4.2) | |
| Donor for liver transplantation | 1 (4.2) | 1 (4.3) | 0 (0) | |
| Abdominal aortic aneurysm | 2 (8.3) | 0 (0) | 1 (4.2) | |
| Obesity | 2 (8.3) | 0 (0) | 0 (0) | |

Values are presented as mean ± SD for quantitative variables and N (%) for qualitative variables.

All 3 groups showed significant increases of ONSD from T10 to T40 compared to baseline (T0). Among the 3 groups, 20 mL group demonstrated the most significant ONSD increase, compared to 5 mL and 10 mL groups. Although the 10 mL group also demonstrated higher increase of ONSD than 5 mL group, it did not show any statistical significance (5 mL group vs. 10 mL group, $P = 0.782$; 5 mL group vs. 20 mL group, $P < 0.001$; 10 mL group vs. 20 mL group, $P < 0.002$, Fig. 3).

At the T20 and T40 time points, the degree of ONSD increase showed to be volume dependent. This means that the 20 mL, 10 mL, and 5 mL groups showed the highest, intermediate, and lowest increase ($P < 0.001$, $P = 0.042$; Table 2, Fig. 3).

The changes of ONSD increase (T10-T0, T20-T0, and T40-T0) among 3 groups demonstrated significant differences. The amount of ONSD increase was most pronounced at T10 and T40. The 20 mL group showed the most significant increase in ONSD ($P < 0.001$, $P = 0.012$, Table 3). All 3 groups showed an $rSO_2$ to be distributed between 60 ~ 70% without any statistical differences (Fig. 4).

Possible complications of increased ICP, such as blurred vision, dizziness, nausea, vomiting, and headache were not found.

## Discussion

This study investigated whether different injection volumes have any influences on the degree of ONSD increase. TEA done with 3 normal saline volumes of normal saline (5 mL, 10 mL and 20 mL) resulted in a significant increase in ONSD, which did not return to baseline level, even 40 minutes after TEA. The highest ONSD value was found at 40 minutes in the 10 mL and 20 mL groups, whereas in the 5 mL group, it was at 20 minutes. At T20 and T40, the 5 mL and 10 mL groups showed more attenuated and gentle slopes of ONSD increase. However, the 20 mL group did not show such attenuation, but did show even higher ONSD increases at T40, compared to T10 and T20. This result implies that 20 mL group might have a significantly longer effect on ICP than that with 5 mL and 10 mL groups. Our study showed significant differences in changes in ONSD over time, following TEA among 3 volumes of normal saline. During the entire study period, the 20 mL group demonstrated the most significant ONSD increases, compared to 5 mL and 10 mL groups. The 20 mL group showed a nearly twofold increase in the degree of changes in ONSD overtime, compared to 5 mL and 10 mL groups. The 10 mL injection group's volume was twice as high as the 5 mL group. However, such twofold increases in ONSD change were not found in the 5 mL and 10 mL

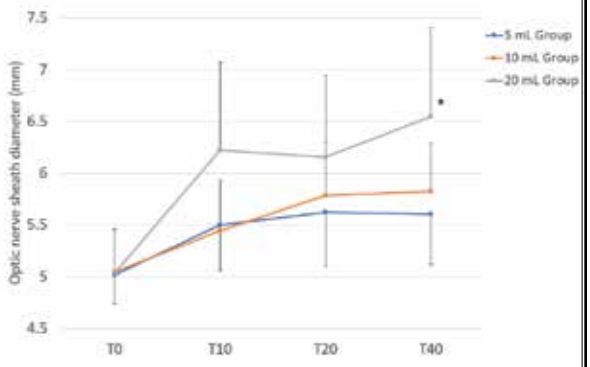


Fig. 3. *Changes in optic nerve sheath diameter (ONSD) according to time. *The 3 groups showed significant differences in changes in ONSD according to time in repeated measure of ANOVA ($P_{group \times time} < 0.001$). Values are mean ± SD. T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection. 5 mL group vs. 10 mL group, P = 0.782; 5ml group vs. 20 ml group, P < 0.001; 10 ml group vs. 20 ml group, P < 0.002.*

Table 2. *Mean Values of optic nerve sheath diameter (ONSD) at each time points.*

| | 5 mL Group (n = 24) | 10 mL Group (n = 23) | 20 mL Group (n = 24) | Adjusted *P*-value |
|---|---|---|---|---|
| ONSD (mm) | | | | |
| T0 | 5.02 ± 0.28 | 5.05 ± 0.41 | 5.04 ± 0.42 | 0.956 |
| T10 | 5.50 ± 0.44 | 5.44 ± 0.49 | 6.22 ± 0.85 | *P* < 0.001 |
| T20 | 5.62 ± 0.52 | 5.78 ± 0.52 | 6.15 ± 0.79 | 0.042 |
| T40 | 5.61 ± 0.49 | 5.83 ± 0.46 | 6.55 ± 0.86 | *P* < 0.001 |

Values are presented as mean ± SD. Adjusted *P*-value indicates the Bonferroni-corrected *P*-value. T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection.

groups. This result implies that if the injection volume does not exceed 10 mL, the degree of changes in ONSD over time can be more attenuated.

Since the optic nerve is closely encircled by the subarachnoid space, an increase in ICP can cause movement of CSF into the perineural subarachnoid space. The subarachnoid space surrounding the optic nerve sheath has an elastic trabecular structure. It is most distensible 3 mm behind the papilla in the globe. Due to such distensibility, the optic nerve sheath inflates within a few minutes of exposure to increased ICP (14,24). Furthermore, previous a study demonstrated

Table 3. *Degree of changes in optic nerve sheath diameter (ONSD) between time points.*

| | 5 mL Group (n = 24) | 10 mL Group (n = 23) | 20 mL Group (n = 24) | Adjusted *P*-value |
|---|---|---|---|---|
| Changes in ONSD (mm) | | | | |
| T10-T0 | 0.49 ± 0.46 | 0.39 ± 0.49 | 1.19 ± 0.89 | *P* < 0.001 |
| T20-T0 | 0.61 ± 0.55 | 0.73 ± 0.55 | 1.12 ± 0.70 | 0.012 |
| T40-T0 | 0.59 ± 0.58 | 0.78 ± 0.51 | 1.51 ± 0.74 | *P* < 0.001 |

Values are presented as mean ± SD. Adjusted *P*-value indicates the Bonferroni-corrected *P*-value. T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection.

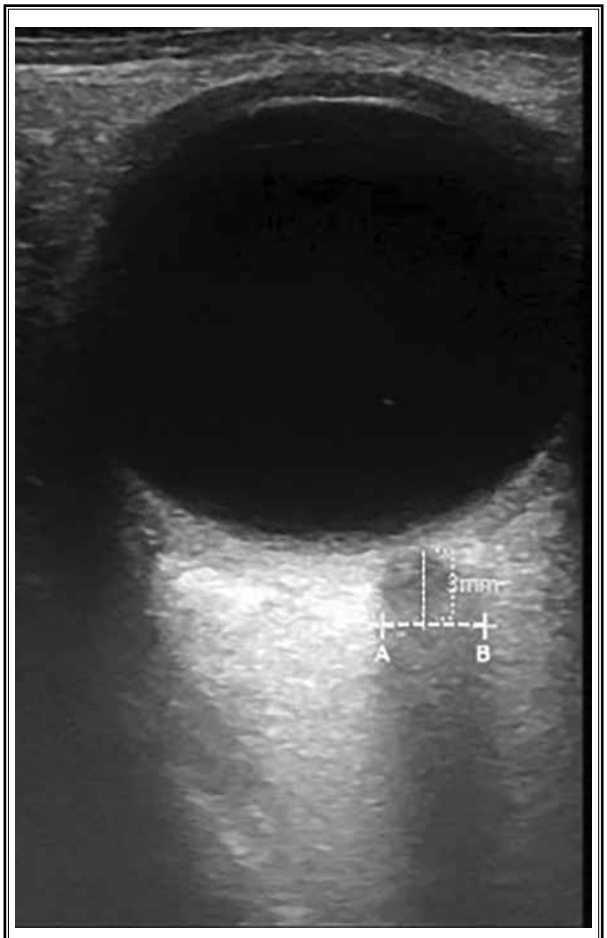


Fig. 4. *Changes in regional cerebral oxygenation ($rSO_2$) according to time. Values are mean (SD). T0, baseline; T10, 10 minutes after epidural normal saline injection; T20, 20 minutes after epidural normal saline injection; T40, 40 minutes after epidural normal saline injection.*

that ONSD measured by ocular ultrasonography correlated with ICP measured by invasive methods (19). Therefore, our results imply that if injected epidural volumes become higher, the degree of increase of ICP becomes more pronounced.

Monitoring of pressure in the epidural space has been reported to reflect real-time changes in ICP. Both epidural and intracranial pressures have been shown to reach peak pressure just after epidural injection and decline thereafter (10,12,25,26). When normal saline or local anesthetics is injected in epidural space, the main factor causing an elevation of ICP is thought to be the movement of CSF from the spinal subarachnoid space to the cranial cavity. Such movement of CSF toward the intracranial space occurs due to a pressure difference between the spinal and intracranial spaces, when normal saline or local anesthetics is injected in the epidural space. This phenomenon has been demonstrated by a previous study, which revealed a bi-directional movement of CSF between the cranial and spinal subarachnoid spaces, according to the pressure gradient (27).

ICP is determined by a dynamic component which is affected by the brain, intracranial blood flow, and CSF (28). If CSF is shifted from the spinal to the intracranial space, this change results in an increased ICP.

Cerebral oxygenation can be monitored by $rSO_2$ and this reflects cerebral perfusion. The $rSO_2$ is comprised of 25% arterial and 75% venous blood according to the manufacturer. The $rSO_2$ represents oxygen saturation of the frontal lobe, but not the whole brain (29). A high-volume caudal block performed in infants fewer than 3 months of age resulted in a biphasic change in cerebral blood flow velocity, with decreased cerebral oxygenation ($rSO_2$) (12). However, our study did not show any significant increase or decrease of $rSO_2$ among the 3 groups. Since the 20 mL group showed the most significant increase of ONSD, compared to the 5 mL or 10 mL group, the $rSO_2$ was expected to be significantly decreased; however, such change in $rSO_2$ was not found in the 20 mL group and the $rSO_2$ showed minimal differences when compared to baseline in all 3 groups.

In a porcine study mimicking epidural anesthesia in adults, ICP and cerebral blood flow were measured following an epidural injection of lidocaine. Their study showed a rapid ICP increase that slowly returned to normal value over a 30-minute period (10); however, the cerebral blood flow showed a rapid reduction followed by a much faster recovery, compared with the ICP response. Significant cerebral blood flow and $rSO_2$ decrease of high volume of caudal block in infants also showed such immediate changes after epidural injection (1 minute) (12). Since $rSO_2$ and cerebral blood flow show faster recovery compared to the ICP response, our study could not represent such fast responses of $rSO_2$. If an $rSO_2$ was measured at 1 minute following normal saline injection, instead of 10 minutes (T10), a different result might be found. Further study is required to measure an $rSO_2$ changes immediately following epidural anesthesia.

### Limitations

Our study includes several limitations. First, we started to measure ONSD and $rSO_2$ values from 10 minutes (T10) following epidural saline injection. Therefore, the investigation of immediate changes to ONSD and $rSO_2$ were limited. Second, the ONSD values measured at T40 did not return to a baseline value. This study could not conclude the time point when ONSD was normalized. Further study is required to confirm the normalizing ONSD time point.

## Conclusion

In conclusion, TEA with 20 mL of normal saline injection resulted in a significant increase in ONSD, compared to the 5mL and 10 mL groups. Our study also indicates that this increase in ONSD occurs in accordance with the injected volume of normal saline. While this effect of increased ICP is unlikely to be harmful in patients without cerebrovascular disease, careful attention should be paid to patients who are at risk of increased ICP, when high volumes of local anesthetics are required for TEA.

## References


1. Groen JV, Khawar AAJ, Bauer PA, et al. Meta-analysis of epidural analgesia in patients undergoing pancreatoduodenectomy. *BJS Open* 2019; 3:559-571.
2. Koul A, Pant D, Rudravaram S, Sood J. Thoracic epidural analgesia in donor hepatectomy: An analysis. *Liver Transpl* 2018; 24:214-221.
3. Yassin HM, Abd Elmoneim AT, El Moutaz H. The analgesic efficiency of ultrasound-guided rectus sheath analgesia compared with low thoracic epidural analgesia after elective abdominal surgery with a midline incision: A prospective randomized controlled trial. *Anesth Pain Med* 2017; 7:e14244.
4. Son WG, Jang M, Jo SM, Kim H, Shin CW, Lee I. Cranial versus caudal thoracic epidural anesthesia using three volumes of lidocaine in conscious Beagle dogs. *Vet Anaesth Analg* 2019; 46:96-105.

5. Hong J, Jung SW. Fluoroscopically guided thoracic interlaminar epidural injection: A comparative epidurography study using 2.5 mL and 5 mL of contrast dye. *Pain Physician* 2016; 19:E1013-1018.
6. Li Y, Dong H, Tan S, Qian Y, Jin W. Effects of thoracic epidural anesthesia/analgesia on the stress response, pain relief, hospital stay, and treatment costs of patients with esophageal carcinoma undergoing thoracic surgery: A single-center, randomized controlled trial. *Medicine (Baltimore)* 2019; 98:e14362.
7. Thepsoparn M, Sereeyotin J, Pannangpetch P. Effects of combined lower thoracic epidural/general anesthesia on pain control in patients undergoing elective lumbar spine surgery: A randomized controlled trial. *Spine (Phila Pa 1976)* 2018; 43:1381-1385.
8. Visser WA, Lee RA, Gielen MJ. Factors affecting the distribution of neural blockade by local anesthetics in epidural anesthesia and a comparison of lumbar versus thoracic epidural anesthesia. *Anesth Analg* 2008; 107:708-721.
9. Lee B, Koo BN, Choi YS, Kil HK, Kim MS, Lee JH. Effect of caudal block using different volumes of local anaesthetic on optic nerve sheath diameter in children: A prospective, randomized trial. *Br J Anaesth* 2017; 118:781-787.
10. Grocott HP, Mutch WA. Epidural anesthesia and acutely increased intracranial pressure. Lumbar epidural space hydrodynamics in a porcine model. *Anesthesiology* 1996; 85:1086-1091.
11. Hong JH, Jung SW, Park JH. The effect of speed of normal saline injection on optic nerve sheath diameter in thoracic epidural anesthesia. *Pain Physician* 2019; 22:E325-e332.
12. Lundblad M, Forestier J, Marhofer D, Eksborg S, Winberg P, Lonnqvist PA. Reduction of cerebral mean blood flow velocity and oxygenation after high-volume (1.5 ml kg(-)(1)) caudal block in infants. *Br J Anaesth* 2014; 113:688-694.
13. Ali MA, Hashmi M, Shamim S, Salam B, Siraj S, Salim B. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure through an external ventricular drain. *Cureus* 2019; 11:e5777.
14. Dubost C, Le Gouez A, Jouffroy V, et al. Optic nerve sheath diameter used as ultrasonographic assessment of the incidence of raised intracranial pressure in preeclampsia: A pilot study. *Anesthesiology* 2012; 116:1066-1071.
15. Ozturk Z, Atalay T, Arhan E, et al. The efficacy of orbital ultrasonography and magnetic resonance imaging findings with direct measurement of intracranial pressure in distinguishing papilledema from pseudopapilledema. *Childs Nerv Syst* 2017; 33:1501-1507.
16. Lee SU, Jeon JP, Lee H, et al. Optic nerve sheath diameter threshold by ocular ultrasonography for detection of increased intracranial pressure in Korean adult patients with brain lesions. *Medicine (Baltimore)* 2016; 95:e5061.
17. Kim SH, Kim HJ, Jung KT. Position does not affect the optic nerve sheath diameter during laparoscopy. *Korean J Anesthesiol* 2015; 68:358-363.
18. Kim JY, Min HG, Ha SI, Jeong HW, Seo H, Kim JU. Dynamic optic nerve sheath diameter responses to short-term hyperventilation measured with sonography in patients under general anesthesia. *Korean J Anesthesiol* 2014; 67:240-245.
19. Padayachy LC, Padayachy V, Galal U, Gray R, Fieggen AG. The relationship between transorbital ultrasound measurement of the optic nerve sheath diameter (ONSD) and invasively measured ICP in children: Part I: Repeatability, observer variability and general analysis. *Childs Nerv Syst* 2016; 32:1769-1778.
20. Cimilli Ozturk T, Demir H, Yorulmaz R, Ozdemir S, Isat G, Ecmel Onur O. Assessment of intra-interobserver reliability of the sonographic optic nerve sheath diameter measurement. *Kaohsiung J Med Sci* 2015; 31:432-436.
21. Hong JH, Jung SW, Park JH. Posture influences the extent of spread of contrast medium during thoracic epidurography: A prospective randomized trial. *Pain Physician* 2017; 20:501-508.
22. Park J, Hong J, Kim J, Yi S. The effect of different posture on normal saline injection in optic nerve sheath diameter in thoracic epidural anesthesia. *Pain Physician* 2020; 23:573-579.
23. Moretti R, Pizzi B. Ultrasonography of the optic nerve in neurocritically ill patients. *Acta Anaesthesiol Scand* 2011; 55:644-652.
24. Robba C, Cardim D, Tajsic T, et al. Ultrasound non-invasive measurement of intracranial pressure in neurointensive care: A prospective observational study. *PLoS Med* 2017; 14:e1002356.
25. Uldall M, Juhler M, Skjolding AD, Kruuse C, Jansen-Olesen I, Jensen R. A novel method for long-term monitoring of intracranial pressure in rats. *J Neurosci Methods* 2014; 227:1-9.
26. Eide PK, Sorteberg W. Simultaneous measurements of intracranial pressure parameters in the epidural space and in brain parenchyma in patients with hydrocephalus. *J Neurosurg* 2010; 113:1317-1325.
27. Klarica M, Rados M, Erceg G, Petosic A, Jurjevic I, Oreskovic D. The influence of body position on cerebrospinal fluid pressure gradient and movement in cats with normal and impaired craniospinal communication. *PLoS One* 2014; 9:e95229.
28. Wilson MH. Monro-Kellie 2.0: The dynamic vascular and venous pathophysiological components of intracranial pressure. *J Cereb Blood Flow Metab* 2016; 36:1338-1350.
29. Matsuoka T, Ishiyama T, Shintani N, Kotoda M, Mitsui K, Matsukawa T. Changes of cerebral regional oxygen saturation during pneumoperitoneum and Trendelenburg position under propofol anesthesia: A prospective observational study. *BMC Anesthesiol* 2019; 19:72.