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The effect of thoracic epidural nerve block with Dezocine and Ropivacaine on arterial oxygen aaturation and IDO gene expression during pulmonary ventilation in lung resection surgery

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ABSTRACT

During lung resection surgery, the blood supply to the lungs increases the intrapulmonary shunt and reduces arterial oxygenation in patients. Ventilation anesthesia of a lung may affect oxygenation. The present study aimed to compare intravenous anesthesia with and without thoracic epidural block (dezocine and ropivacaine) on oxygen saturation during lung ventilation in patients undergoing lung resection surgery. For this purpose, this study was performed as a double-blind, randomized clinical trial. Sixty patients who were candidates for lung resection were divided into two intervention groups (thoracic epidural block with dezocine and ropivacaine and intravenous anesthesia) and a control group (placebo thoracic epidural block and intravenous anesthesia). Hemodynamic variables, Aldert score, and possible complications were compared between the two groups before surgery and after recovery. Also, the expression level of the IDO gene was evaluated using the real-time PCR technique. SPSS, t-test, Mann-Whitney U, Chi-square, and Fisher performed data analysis and comparison. The results showed that the changes in hemodynamic variables and PaO_2, SaO_2, and $ETCO_2$ were not statistically significant between the two groups. Aldrete's score at entry and exit of recovery was similar between the two groups. During the recovery period, the percentage of pain or chills in the group under complete intravenous anesthesia was significantly higher. There was no significant difference between the two groups regarding the frequency of nausea and hypotension. Also, the results of IDO gene expression showed that general anesthesia with the thoracic epidural block (dezocine and ropivacaine), which is involved in inducing immunological tolerance and suppressing immune responses, has no significant effect. The stress of performing surgery before surgery can play a role in suppressing the patient's immunity, and anesthesia of the thoracic epidural block (dezocine and ropivacaine) has no significant effect on IDO expression. In general, thoracic epidural block with complete intravenous anesthesia has no significant effect on oxygen saturation in ventilated lungs compared with intravenous anesthesia alone. Nevertheless, this combination significantly reduces postoperative pain and chills.

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Introduction

Pulmonary ventilation is commonly used during thoracic surgery. With the onset of ventilation in a lung, blood from hypoxic areas in the unventilated lung to the ventilated lung improves oxygenation by reducing the mismatch in the ventilation/blood flow ratio (1). The cause of this condition is Hypoxic Pulmonary Vasoconstriction (HPV). Numerous factors affect HPV, either directly (such as inhaled anesthetics, vasodilators such as tri-nitroglycerin and sodium nitroprusside, hypercarbia, blood pH, lung manipulation, and epidural block) or indirectly (such as epinephrine and phenylephrine) (2). Many studies have shown that HPV can be inhibited by inhaled anesthetics, especially halothane and isoflurane (3). The vasodilatory effects of these drugs inhibit physiological changes in blood flow when ventilating a lung, increasing shunting and reducing arterial blood oxygen saturation (4). On the other hand, intravenous anesthetics and Total Intravenous Anesthesia using propofol and short-acting narcotics have been shown to have no inhibitory effect on HPV. Intravenous anesthetics are a good determinant of compliance between ventilation and perfusion during anesthesia (5).

A thoracic epidural block is an excellent method for controlling acute pain after thoracotomy. It has a known role in improving cardiopulmonary and gastrointestinal function (6). Thoracic epidural block reduces heart rate and cardiac output, dilates the pulmonary and systemic arteries, and reduces moderate arterial pressure and oxygen saturation of the venous mixture (7). As local amide anesthetics, ropivacaine has dual analgesia and anesthesia impacts, with low cardiotoxicity and neurotoxicity. Considers have appeared that ropivacaine is secure and viable for postoperative analgesia (8). As an opioid receptor agonist-antagonist, dezocine can effectively overcome the abuse and body dependence caused by pure opioids, which have an excellent analgesia impact and insignificant effect on the gastrointestinal tract and respiratory system (9).

Recent studies have shown that kynurenine pathway metabolites suppress the immune response (10, 11). The

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primary enzyme controlling this pathway is indoleamine 2,3-dioxygenase (IDO). IDO is an intracellular enzyme that prevents the breakdown of tryptophan in the kynurenine pathway (12). Evaluations have shown that general anesthesia affects IDO gene expression, induction of immunological tolerance, and suppression of immune responses (13).

According to the above, this study aimed to evaluate the anesthesia effect of the thoracic epidural block with dezocine and ropivacaine on arterial oxygen saturation and IDO gene expression during pulmonary ventilation in lung resection surgery.

Materials and Methods

Studied patients

This study is a double-blind and prospective randomized clinical trial. Sixty patients who were candidates for lung resection surgery were randomly divided into two groups of 30 patients. The intervention group (under TIVA and thoracic epidural block with dezocine and ropivacaine) and the control group (under TIVA and thoracic epidural block with normal saline) were evaluated thoracic surgery ward. Inclusion criteria in the study included patients with lung tumors who were candidates for elective lung resection surgery with single lung ventilation. Exclusion criteria included patients with spinal anomalies, neurological disorders, known cardiovascular disease, anemia, renal or hepatic insufficiency, coagulation disorders, and diabetes. Sampling was done by easy method one after the other and based on the order of patients' referrals.

Experimental evaluations

After sufficient explanation, written consent was obtained from all patients. Patients did not receive any pretreatment before entering the operating room. Before the start of anesthesia, pre-treatment was midazolam 0.015 mg/kg body weight for all patients. Before induction of anesthesia, an epidural catheter was inserted from space T5-T6, 20 to 30 minutes before anesthesia. Patients in the control group underwent placebo epidural block (normal saline + TIVA), and patients in the intervention group underwent thoracic epidural block (dezocine and ropivacaine + TIVA).

Induction of anesthesia was performed at a rate of 10 mg/s of intravenous propofol. This process was continued until Bispectral Index (BIS) reached below 50. Anesthesia was maintained with the infusion of propofol and remifentanil 10-20 µg/kg/h at a rate of BIS below 45 ± 5. All conditions were the same in the two groups. Patients were intubated with a left-handed PVC bi-duct tube. One minute after intubation, the drug (dezocine and ropivacaine) or placebo (normal saline) was injected through an epidural catheter. Patients were monitored, including CVP, ECG, BP, SaO_2, and urinary output for up to half an hour every 5 minutes and then every 15 minutes. Reduction of blood pressure by more than 30% of baseline blood pressure was considered hypotension, and, if necessary, intravenous ephedrine was prescribed.

The anesthesia and ventilation of patients remained the same. The duration of extubation (from drug discontinuation to extubation) and the recovery time (from extubation to Aldrete Scoring; patients' discharge criteria based on activity, respiration, blood circulation, color, and alertness) were calculated. In the placebo group, the postoperative epidural catheter was used for analgesia. The drug used was 125% marcaine with 1 mg of morphine per 5 ml of local anesthetic solution and infusion at a 5 ml/hour rate. All patients were visited by an anesthesia assistant every 6 hours until 24 hours later to monitor for possible complications. Hemodynamic parameters (mean blood pressure and heart rate) and PaO_2, SaO_2, and $ETCO_2$ were recorded before and after epidural injection, before induction, immediately after intubation, 5 minutes to 60 minutes after intubation, and immediately before pulmonary injection, and during recovery and after recovery.

Expression of indoleamine 2, 3-dioxygenase gene

Five milliliters of peripheral blood were obtained from all sixty patients in both the intervention and control group. The extraction was performed according to the RNA extraction kit protocol (Qiagen, South Korea). After RNA extraction, the cDNA was synthesized by Vivantis cDNA synthesis kit (Malaysia). Specific primer pairs were designed to amplify the sequences of indoleamine 2, 3-dioxygenase (IDO) gene and GAPDH gene (internal control). The primers were designed using Gene Runner 5 and Primer Express 1.0.3 software. Table 1 shows the sequence of primers for the real-time PCR technique.

The final volume for each reaction was 20µl, including 100ng of Power SYBR® Green PCR Master, 1µl of cDNA, 10µl of Master Mix (Applied Biosystems, USA), 10mmol/µl of primers, and 6µl of nuclease-free water. Temperature protocol was performed as initial denaturation at 95°C for 3 minutes. Subsequently, 45 cycles were performed as denaturation at 95°C for 5 seconds and annealing at 60°C for 30 seconds. Reproduction analysis and melting curve were performed using Applied Biosystems 7500. Then gene expression diagram was drawn using Prism 5 GraphPad software.

Statistical analysis

The obtained information was expressed in Mean ± SD, frequency, and percentage. The statistical program used was SPSS. Quantitative variables were compared using a t-test or a Mann-Whitney U test. The comparison of qualitative variables was made by Contingency Tables using the Chi-square test or Fisher's exact test according to the conditions. Repeated Measures analysis compared quantitative parameter changes between the two groups.

Table 1. The Primer sequences of IDO and GAPDH genes for the Real-time PCR technique.a

Gene	Primer Sequence (5'-3')	Product size
IDO (Forward)	GTGTTTCACCAAATCCACGA	124bp
IDO (Reverse)	CTGATAGCTGGGGGTTGC	
GAPDH (Forward)	TGCACCACCAACTGCTTAGC	85bp
GAPDH (Reverse)	GGCATGGACTGTGGTCATGAG	

In all cases studied, the results were statistically significant if they had a $p \leq 0.05$. Also, genetic data analysis was performed based on threshold cycle comparison (Ct). The ΔCT was calculated by the Ct difference obtained from the tested samples. Then, it was calculated using the formula $2^{-\Delta\Delta CT}$.

Results and discussion

The mean age of patients in the intervention group was 50.5 ± 14.6 years, and the mean age of patients in the control group was 48.3 ± 18.2 years. There was no statistically significant difference between the two groups (p = 0.607). In the intervention group, 20 patients (66.7%) were male, and ten patients (33.3%) were female. Twenty-two patients (73.3%) were male in the control group, and eight patients (26.7%) were female. There was no statistically significant difference between the two groups (p = 0.573). The mean weight of patients in the intervention group was 64.3 ± 9.3 kg, and the mean weight of patients in the control group was 68.8 ± 10.2 kg. There was no statistically significant difference between the two groups (p = 0.075).

The mean ASA in patients in the intervention group was 1.5 ± 0.6, and the mean ASA in patients in the control group was 1.3 ± 0.5. There was no statistically significant difference between the two groups (p = 0.064). The mean duration of operation in the intervention group was 197.7 ± 54.6 minutes, and the mean duration of operation in the control group was 195.0 ± 54.6 minutes. There was no statistically significant difference between the two groups (p = 0.841). The changes in mean, mean blood pressure from the beginning to the end of the study in the two groups are shown in Figure 1. Accordingly, no statistically significant difference was observed between the two groups (p = 0.084). Mean changes in mean blood pressure after the onset of pulmonary ventilation were not statistically significant between the two groups (p = 0.531).

The changes in mean heart rate from the beginning to the end of the study in the two groups are shown in Figure 2. No statistically significant difference was observed between the two groups (p = 0.429). Mean changes in heart rate after the onset of pulmonary ventilation were not statistically significant between the two groups (p = 0.481).

The mean changes of SaO_2 from the beginning to the end of the study in the two groups are shown in Figure 3. No statistically significant difference was observed between the two groups (p = 0.061). Mean changes of SaO_2 after the onset of single pulmonary ventilation were not statistically significant between the two groups (p = 0.159). Mean changes in PaO_2 after the beginning of pulmonary ventilation were not statistically significant between the two groups (p = 0.510).

The mean changes in $ETCO_2$ from the beginning to the end of the study in the two groups are shown in Figure 4. Accordingly, no statistically significant difference was observed between the two groups (P = 0.287). Mean changes in $ETCO_2$ after the onset of pulmonary ventilation were not statistically significant between the two groups (p = 0.581).

At the time of recovery, the mean Aldrete score in the intervention group was 7.7 ± 0.6, and in the control group was 6.7 ± 1.2. Aldrete's mean score when entering recovery was significantly higher in the intervention group (p <0.001). The mean Aldrete score at recovery time was 9.9 ± 0.3 (median 10, range 9 to 10) in the intervention group, and 10.0 ± 0.0 in the control group. There was no statis-

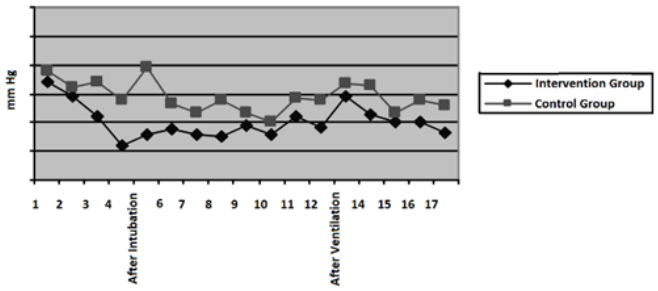

Figure 1. The average changes in mean blood pressure during the study in two intervention and control groups.

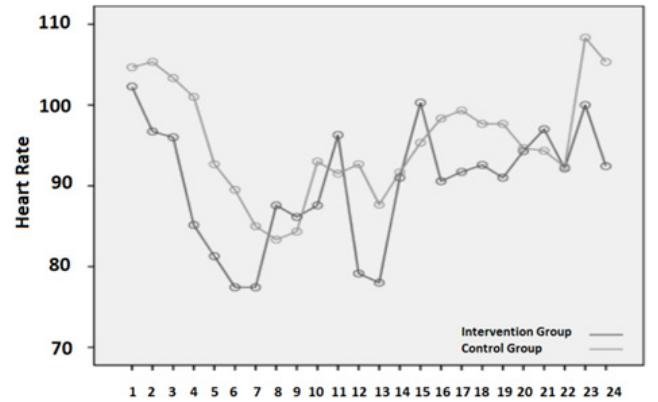

Figure 2. Changes in mean heart rate during the study in the intervention and control groups.

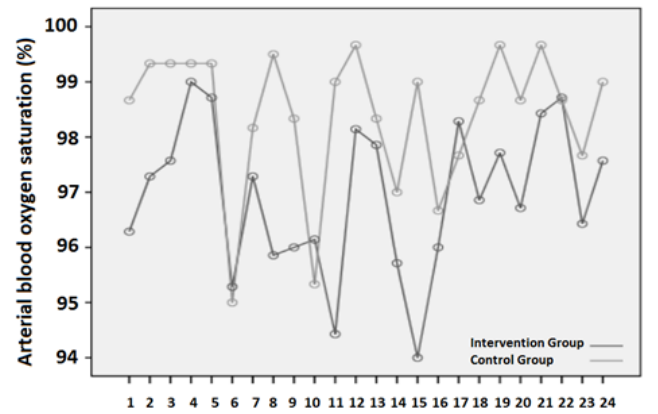

Figure 3. Mean changes in SaO_2 during the study in the intervention and control groups.

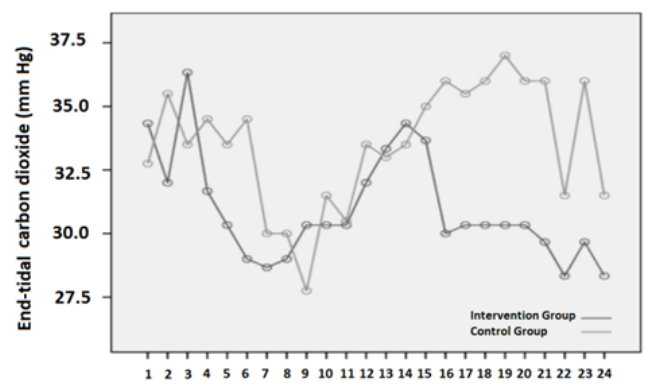

Figure 4. Mean $ETCO_2$ changes during the study in the intervention and control groups.

tically significant difference between the two groups (p = 0.155).

The mean length of stay in recovery was 22.4 ± 4.9 minutes in the intervention group and 22.9 ± 5.1 minutes in the control group. There was no statistically significant difference between the two groups (p = 0.738).

In the intervention group, pain, nausea, chills, and hypotension were seen in 7 (23.3%), 0 (0%), 1 (3.3%), and 1 (3.3%) patients in intervention group, and 25 (83.3%), 1 (3.3%), 10 (33.3%), and 0 (0%) in the control group, respectively. Therefore, the percentage of cases of pain and chills in recovery in the control group was significantly higher than in the intervention group. None of the patients developed arrhythmias or hypertension during their stay in recovery. The mean total dose of propofol during surgery was 1.12 ± 0.58 mg/kg in the intervention group and 1.67 ± 0.46 mg/kg in the control group. There was a statistically significant difference between the two groups (p = 0.0384).

The mean total dose of remifentanil during surgery was 2137.7 ± 0.741 µg in the intervention group and 2234.2 ± 612.2 µg in the control group. There was no statistically significant difference between the two groups (p = 0.584).

The results of IDO gene expression showed that there was no statistically different between the intervention group and control group, before (p = 0.834) and after (p = 0.212) intervention (Figure 5).

Several factors affect oxygenation when a lung is ventilated. Anesthesia is one of these factors. A thoracic epidural block is an excellent method for controlling acute pain after thoracotomy and has a known role in improving cardiopulmonary and gastrointestinal function (14). Thoracic epidural block reduces heart rate and cardiac output, dilates pulmonary and systemic arteries, and reduces moderate arterial pressure and oxygen saturation of the venous mixture (15). Previous studies have shown conflicting information about the thoracic epidural block's effect on oxygenation during lung ventilation (16-18).

This prospective study showed that thoracic epidural block combined with complete venous anesthesia did not affect oxygenation during lung ventilation. In this study, we compared the effect of the thoracic epidural block (dezocine and ropivacaine) combined with complete intravenous anesthesia (propofol + remifentanil) on arterial oxygen saturation during ventilation of a lung.

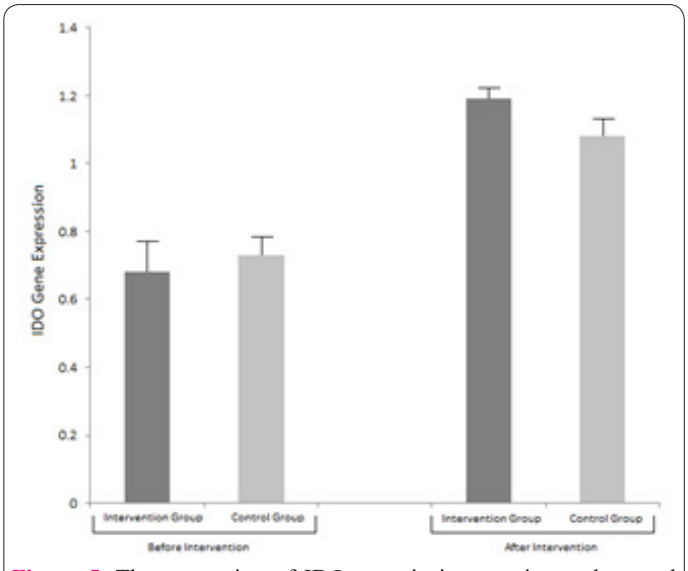

Figure 5. The expression of IDO gene in intervention and control group before and after intervention.

Accordingly, changes in HR, $EtCO_2$, SaO_2, PaO_2, and BP after the onset of pulmonary ventilation were not statistically significant in the two groups. In a study by Choi *et al*. (19) compared thoracic epidural block with general anesthesia to arterial oxygen saturation during lung ventilation (15 and 30 minutes later). In this study, 30 patients in each group were studied. Based on this, it was shown that the mean arterial oxygen saturation was significantly higher in the measured sections in the general anesthesia group. Finally, it was concluded that thoracic epidural block combined with general anesthesia reduces arterial oxygen saturation and increases arterial-venous shunt.

In another study by Wang *et al*. (20), 50 patients in two groups were studied. In one group, complete intravenous anesthesia was used; in the second group, thoracic epidural block with general anesthesia. In comparison between the two groups, the thoracic epidural block had no significant effect on arterial oxygenation. Based on this, it was concluded that the thoracic epidural block with general anesthesia is superior to general anesthesia.

In another similar study by Ishibe *et al*. (21), it was shown that adding a thoracic epidural block to general anesthesia compared to the general anesthesia group only increased arterial oxygenation after ventilation of a lung and was therefore recommended.

In a study by Chow *et al*. (22) on 34 patients, complete intravenous anesthesia was used alone in one group. The thoracic epidural block (bupivacaine) was used in the second group under general anesthesia. During ventilation of one lung, no statistically significant difference was reported in terms of arterial oxygenation and arteriovenous shunt between the two groups. In another study by Garutti *et al*. (23), 72 patients were studied in two groups. In one group, general anesthesia was used alone, and in the other group, general anesthesia with the thoracic epidural block (meperidine) was used. After ventilation of one lung, no significant difference was observed in terms of arterial oxygenation between the two groups. In another study, Ozcan *et al*. (24) compared 100 patients in four groups. In these patients, complete venous anesthesia, complete venous anesthesia with the thoracic epidural block (bupivacaine), inhalation anesthesia (isoflurane), and inhalation anesthesia with thoracic epidural block were used. Finally, it was shown that there was no statistically significant difference in terms of oxygenation and arteriovenous shunt after ventilation of one lung between these four groups. As can be seen, the results of studies in this field are very variable and contradictory. In conclusion, in pulmonary ventilation, the use of thoracic epidural block combined with general anesthesia (intravenous or inhalation) has either worsened the oxygenation status, improved the patient's condition, or has not had a significant effect (21-24). Therefore, the present study is in line with the third category of studies. Numerous cases have been suggested to justify the differences in the results of different studies in this field. One of these cases is the effect of the type of drug used in the thoracic epidural block (25).

Different effects of opioids and local anesthetics have been reported, with opioids causing pain without affecting the sympathetic system (26). In contrast, local anesthetics can block the sympathetic system in addition to causing analgesia (27).

Due to the autonomic system's innervation of the pul-

monary arteries, HPV may be affected by the sympathetic block (3). However, Garutti *et al*. (23) did not endorse such a mechanism in their study. In another study by Jung *et al*. (28), the drug used in thoracic epidural block (opioid or local anesthetic) did not affect HPV during lung ventilation. Previous studies in animal models and patients undergoing lung transplantation have shown that HPV is not affected by the autonomic (sympathetic) system (4). Other cases suggested justifying the variable results of various studies include differences in regimens used for general anesthesia (intravenous or inhalation), amount and dose of drugs used for thoracic epidural block, age of patients (independent factor), PaO_2 before Ventilation of a lung (independent factor) and how to assess the amount of arterial oxygenation after ventilation of a lung (15).

There was no statistically significant difference in hemodynamic changes (heart rate and mean blood pressure) during the study period between the two groups in the present study. At the same time, the frequency of pain and chills during recovery was significantly lower in the group under intravenous anesthesia and thoracic epidural block than in the group under intravenous anesthesia alone. In the study of Garutti *et al*. (23), no statistically significant difference in terms of hemodynamic status (heart rate and mean blood pressure) was reported between the two groups. In the study of Jung *et al*. (28), a similar result was declared. In their research, Chow *et al*. (22) did not report a statistically significant difference in terms of hemodynamic changes after ventilation of one lung between the two groups. As can be seen, the present study in this field has been in line with the mentioned studies.

On the other hand, Rodgers *et al*. (29) in a meta-analysis concluded that neuraxial block in a ventilated lung significantly reduces mortality and postoperative complications. Ballantyne *et al*. (30) also showed in their study that thoracic epidural block combined with general anesthesia could improve the prognosis of patients after lung ventilation. The results of this study also confirmed these results.

In our study, the results of the gene expression study showed that general anesthesia with the thoracic epidural block (dezocine and ropivacaine), which is involved in inducing immunological tolerance and suppressing immune responses, has no significant effect. The stress of performing surgery before surgery can play a role in suppressing the patient's immunity, and anesthesia of the thoracic epidural block (dezocine and ropivacaine) has no significant effect on IDO expression.

In general, changes in BP, HR, $ETCO_2$, SaO_2, and PaO_2 of pulmonary ventilation were not statistically significant in thoracic epidural block (dezocine and ropivacaine) and in placebo thoracic epidural block. Pain and chills during recovery were significantly lower in the intravenous anesthesia group (TIVA) with thoracic epidural block than in the intravenous anesthesia group (TIVA) with placebo thoracic epidural block. The thoracic epidural block (dezocine and ropivacaine) is superior to placebo in recovery complications.

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Authors' contribution
This study was done by the authors named in this article, and the authors accept all liabilities resulting from claims which relate to this article and its contents.

Interest conflict
The authors declare that they have no conflict of interest.

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Availability of data and materials
The data used to support the findings of this study are available from the corresponding author upon request.

Statements and declarations
The author declares that no conflict of interest is associated with this study.

References

1. Garcia Parraga D, Moore M, Fahlman A. Pulmonary ventilation–perfusion mismatch: a novel hypothesis for how diving vertebrates may avoid the bends. Proc R Soc B: Biol Sci 2018; 285(1877): 20180482.
2. Dunham-Snary KJ, Wu D, Potus F et al. Ndufs2, a core subunit of mitochondrial complex I, is essential for acute oxygen-sensing and hypoxic pulmonary vasoconstriction. Circ Res 2019; 124(12): 1727-1746.
3. Smith KA, Schumacker PT. Sensors and signals: the role of reactive oxygen species in hypoxic pulmonary vasoconstriction. J Physiol 2019; 597(4): 1033-1043.
4. Licker M, Hagerman A, Jeleff A, Schorer R, Ellenberger C. The hypoxic pulmonary vasoconstriction: From physiology to clinical application in thoracic surgery. Saudi J Anaesth 2021; 15(3): 250.
5. Strielkov I, Krause NC, Sommer N et al. Hypoxic pulmonary vasoconstriction in isolated mouse pulmonary arterial vessels. Exp Physiol 2018; 103(9): 1185-1191.
6. Loop T. Does thoracic epidural anaesthesia constitute over-instrumentation in video-and robotic-assisted thoracoscopic lung parenchyma resections? Curr Opin Anaesthesiol 2021; 34(2): 199-203.
7. Liang X-L, An R, Chen Q, Liu H-L. The analgesic effects of thoracic paravertebral block versus thoracic epidural anesthesia after thoracoscopic surgery: A meta-analysis. J Pain Res 2021; 14: 815.
8. Medina M, Foiles SR, Francois M et al. Comparison of cost and outcomes in patients receiving thoracic epidural versus liposomal bupivacaine for video-assisted thoracoscopic pulmonary resection. Am J Surg 2019; 217(3): 520-524.
9. Feltracco P, Bortolato A, Barbieri S et al. Perioperative benefit and outcome of thoracic epidural in esophageal surgery: a clinical review. Dis Esophagus 2018; 31(5): dox135.
10. Nguyen DJ, Theodoropoulos G, Li Y-Y et al. Targeting the kynurenine pathway for the treatment of cisplatin-resistant lung cancer. Mol Cancer Res 2020; 18(1): 105-117.
11. Guo X, Yin B, Wang C, Huo H, Aziziaram Z. Risk assessment of gastric cancer in the presence of Helicobacter pylori cagA and hopQII genes. Cell Mol Biol 2021; 67(4): 299-305.
12. Badawy AA, Guillemin G. The plasma [kynurenine]/[tryptophan] ratio and indoleamine 2, 3-dioxygenase: time for appraisal. Int J Tryptophan Res 2019; 12: 1178646919868978.
13. Mandarano M, Bellezza G, Belladonna ML et al. Indoleamine 2, 3-dioxygenase 2 immunohistochemical expression in resected

human non-small cell lung cancer: a potential new prognostic tool. Front immunol 2020; 11: 839.
14. Hannon CP, Keating TC, Lange JK, Ricciardi BF, Waddell BS, Della Valle CJ. Anesthesia and analgesia practices in total joint arthroplasty: a survey of the American Association of Hip and Knee Surgeons membership. J Arthroplasty 2019; 34(12): 2872-2877. e2872.
15. Hagerman A, Licker M. Anesthesia, Mechanical Ventilation, and Hypoxic Pulmonary Vasoconstriction. *Cohen's Comprehensive Thoracic Anesthesia*: Elsevier; 2022: 193-212.
16. Senturk M. Acute and chronic pain after thoracotomies–editorial review. Curr Opin Anaesthesiol 2005; 18(1): 1-4.
17. Spies C, Zaune U, Pauli M, Boeden G, Martin E. A comparison of enflurane and propofol in thoracic surgery. Der Anaesthesist 1991; 40(1): 14-18.
18. Wang M-L, Hung M-H, Chen J-S, Hsu H-H, Cheng Y-J. Nasal high-flow oxygen therapy improves arterial oxygenation during one-lung ventilation in non-intubated thoracoscopic surgery. Eur J Cardiothorac Surg 2018; 53(5): 1001-1006.
19. Choi H, Jeon J, Huh J, Koo J, Yang S, Hwang W. The effects of iloprost on oxygenation during one-lung ventilation for lung surgery: a randomized controlled trial. J Clin Med 2019; 8(7): 982.
20. Wang Y, Kong L, Liu X. Effect of epidural block anesthesia combined with general anesthesia on postoperative cognitive ability of elderly patients undergoing thoracoscopic surgery. Int J Clin Exp Pathol 2020; 13(10): 2447.
21. Ishibe Y, Shiokawa Y, Umeda T, Uno H, Nakamura M, Izumi T. The effect of thoracic epidural anesthesia on hypoxic pulmonary vasoconstriction in dogs: an analysis of the pressure-flow curve. Anesth Analg 1996; 82(5): 1049-1055.
22. Chow MY-H, Goh M-H, Boey SK, Thirugnanam A, Ip-Yam PC. The effects of remifentanil and thoracic epidural on oxygenation and pulmonary shunt fraction during one-lung ventilation. J Cardiothorac Vasc Anesth 2003; 17(1): 69-72.
23. Garutti I, Cruz P, Olmedilla L et al. Effects of thoracic epidural meperidine on arterial oxygenation during one-lung ventilation in thoracic surgery. J Cardiothorac Vasc Anesth 2003; 17(3): 302-305.
24. Özcan P, Şentürk M, Sungur Ulke Z et al. Effects of thoracic epidural anaesthesia on pulmonary venous admixture and oxygenation during one-lung ventilation. Acta Odontol Scand 2007; 51(8): 1117-1122.
25. Pintaric TS, Potocnik I, Hadzic A, Stupnik T, Pintaric M, Jankovic VN. Comparison of continuous thoracic epidural with paravertebral block on perioperative analgesia and hemodynamic stability in patients having open lung surgery. Reg Anesth Pain Med 2011; 36(3): 256-260-256-260.
26. Elsabeeny WY, Ibrahim MA, Shehab NN, Mohamed A, Wadod MA. Serratus anterior plane block and erector spinae plane block versus thoracic epidural analgesia for perioperative thoracotomy pain control: a randomized controlled study. J Cardiothorac Vasc Anesth 2021; 35(10): 2928-2936.
27. Shanthanna H, Busse J, Wang L et al. Addition of corticosteroids to local anaesthetics for chronic non-cancer pain injections: a systematic review and meta-analysis of randomised controlled trials. Br J Anaesth 2020; 125(5): 779-801.
28. Jung SM, Cho CK, Kim YJ et al. The effect of thoracic epidural anesthesia on pulmonary shunt fraction and arterial oxygenation during one-lung ventilation. J Cardiothorac Vasc Anesth 2010; 24(3): 456-462.
29. Rodgers A, Walker N, Schug S et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. Bmj 2000; 321(7275): 1493.
30. Ballantyne JC, Carr DB, deFerranti S et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. Anesth Analg 1998; 86(3): 598-612.