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Challenge Journal of Perioperative Medicine

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Challenge Journal of Perioperative Medicine

Research Article

# The effects of lycopene in lung injury associated with cecum ligation and perforation-induced sepsis in rats: An investigative animal experiment study

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## ABSTRACT

**Background:** The primary aim of this study is to evaluate the effect of lycopene on serum interleukin-1ß (IL-1ß) and interleukin-6 (IL-6) levels in rats subjected to sepsis induced by the cecal ligation and perforation (CLP) method, as well as to assess the impact of lycopene on inflammation in the lungs, which is the first organ affected by sepsis.

**Methods:** Twenty-four male rats were divided into four groups - control (healthy group), sepsis (CLP group), sepsis + lycopene 100 mg/kg (L100 group), and sepsis + lycopene 200 mg/kg (L200 group). Lycopene was administered by gastric lavage at doses of 100 mg/kg to the L100 group and 200 mg/kg to the L200 group. Intracardiac blood samples were collected 18 h after CLP for serum IL-1β and IL-6 level analysis. Lung tissue specimens were also collected for histopathological examination.

**Results:** IL-1β levels decreased significantly in the L100 and L200 groups compared to the CLP group ($p<0.001$). Both doses of lycopene statistically significantly reduced serum IL-6 levels in the L100 and L200 groups compared to the CLP group. Serum IL-6 levels also decreased significantly in the L200 group compared to the L100 group ($p<0.001$).The degree of inflammation, vascular congestion and edema decreased significantly in the L200 group compared to the CLP group ($p<0.001$).

**Conclusion:** Use of lycopene in rats with CLP-induced sepsis reduced serum IL-1β and IL-6 levels and inflammation in lung tissue at histopathological examination. Lycopene can be more effective at a dosage of 200 mg/kg.

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## 1. Introduction

Sepsis is a systemic and irregular inflammatory response to infection that is capable of causing hemodynamic instability, multiple organ dysfunction syndrome (MODS), and even death. Sepsis-related mortality rates may sometimes be very high [1]. Also, it is believed that sepsis is more prevalent than is currently being reported because it causes different clinical manifestations and its reporting is not compulsory in some countries [2]. There are several causes for the high rate of mortality among septic patients. These include intravas-

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cular or urinary catheterization; invasive procedures such as endotracheal intubation, which is done when necessary; antibiotic resistance; and high immune suppression, which is associated with therapeutic protocols [1,3].

The course of a disease when sepsis occurs generally depends on the emergence of sepsis-related MODS. Impaired microcirculation due to endothelial damage and the widespread release of inflammatory mediators can lead to the development of MODS [4,5].

Multiple mediators are involved in the pathogenesis of sepsis—including the inflammatory mediator interleukin (IL), tumor necrosis factor (TNF), arachidonic acid, and platelet-activating factor. Also, monocytes, macrophages, and mast and endothelial cells release cytokines against bacteria and endotoxins. TNF-α, interferon-gamma (IF γ), and IL 1β, IL-6, and IL-8 are involved as proinflammatory cytokines in the pathogenesis of sepsis, while IL 10 serves a basic anti-inflammatory cytokine. The blood levels of these mediators increase in sepsis, and the complex relationship between them is gradually being unraveled [6,7] .

Lycopene is a member of the carotenoid family with a powerful antioxidant property because of its conjugated double bonds [8,9]. Due to its nature as a potent anti-inflammatory and antioxidant molecule, we hypothesized that lycopene might be beneficial in the treatment of sepsis and sepsis-related lung damage.

This study was planned to investigate the effectiveness of lycopene in the treatment of sepsis. This study primarily aimed to evaluate the effect of lycopene on IL-1β and IL-6 levels in rats induced with sepsis using the cecum ligation and perforation (CLP) method and assess the level of inflammation in the lungs, which is the first organ affected in sepsis. The secondary aim of the study was to compare the effects of different doses of lycopene on inflammation.

## 2. Materials and Methods

### *2.1. Animal models*

Atatürk University Animal experiments were carried out with the decision of the local ethics committee dated 27.12.2018, number 13, decision number 235. Twenty-four male albino Wistar rats weighing 220–250 g obtained from the University Medical Experimental Application and Research Centre Laboratory were used for the experiment, which was conducted in the same laboratory. During the experiment, rats were allowed ad libitum access to water and chow (complete mouse and rat feed: raw protein 23%, raw ash 8%, raw cellulose 7%, and raw fat 3%; Bil-yem, Ankara, Turkey). Before the experiment, the animals were housed in the laboratory in groups in standard cages with sawdust flooring at normal room temperature (22–25 °C) and in a 12 h light/12 h dark cycle. Access to water alone was permitted 12 h before and after the experiment.

Polymicrobial sepsis was induced in healthy rats using the CLP model. For that purpose, the rats were anesthetized with a combination of 75 mg/kg ketamine and 5 mg/kg xylazine. The rats were placed in the supine position while the abdominal region was shaved and cleansed with a 10% povidone-iodine solution. A two cm abdominal midline incision was first made. Then the cecum was located and explored through the anterior muscles of the abdominal wall. The cecum was ligated with 3/0 silk distally to the ileocecal valve in such a way as not to impair blood flow or intestinal circulation. Four holes were made in the cecum (one from one side and one from the opposite side) with the help of an 18-gauge needle, and one part of the cecum content was exteriorized. The abdomen was washed with one ml saline solution and then closed with a 3/0 synthetic absorbable sterile suture.

### *2.2. Study design*

The rats were randomly assigned into groups containing six animals each.

1. Control group (group healthy; n=6): No procedure was performed on the animals in this group to determine the investigated parameters in normal healthy animals. Intracardiac blood and lung tissue specimens were collected immediately after sacrificing the rats.
2. Sepsis group (CLP group; n=6): CLP was performed on this group to induce intra-abdominal sepsis.
3. Sepsis + lycopene 100 mg/kg group (L100 group; n=6): Lycopene (100 mg/kg) was administered by gastric lavage.
4. Sepsis + lycopene 200 mg/kg group (L200 group; n=6): Lycopene (200 mg/kg) was administered by gastric lavage.

The rats were sacrificed 18 h after the induction of sepsis and intracardiac blood and lung tissue specimens were collected immediately after the sacrifice group CLP, L100 and L200.

### *2.3. Chemicals*

Lycopene (DSM, RedivivoTM [lycopene] 10% fluid suspension, Basel, Switzerland) was administered by gastric lavage at dosages of 100 mg/kg and 200 mg/kg to the rats in the L100 and the L200 groups, respectively.

### *2.4. Serum IL-1β and IL-6 level measurement*

Approximately 4–6 cc of blood was collected to measure IL-1β and IL-6. The blood specimens were centrifuged for 10 min at 4000 rpm to separate the serum. The serum specimens were then placed in Eppendorf tubes and stored at -80°C until the day they were analyzed. Serum IL-1β and IL-6 levels were determined using rat IL-1β enzyme-linked immunosorbent assay (Invitrogen, USA; Code: KRC0011) and IL-6 ELISA (Invitrogen, USA; Code: KRC0061) kits, respectively. Unit values were expressed as pg/ml.

### *2.5. Histological procedures*

The lungs of the rats were removed by opening the diaphragm. They were then placed in 10% neutral formaldehyde and sent to the pathology laboratory for his-

topathological examination. All the conventional light microscopy procedures were carried out at the Atatürk University Medical Faculty Pathology Department laboratory. At the end of the experiment, the lung tissues were fixed in 10% formalin solution for 48–55 h. The tissues were dehydrated by passing them through increasing alcohol series and then cleared with xylene series. Following the histopathological procedures, the tissues were embedded in paraffin and cut into five nm-thick sections using a microtome (Leica RM2235, Leica Instruments, Nussloch, Germany) with single-use microtome blades (Leica 819, Leica Instruments, Nussloch, Germany). The tissues were then stained with hematoxylin and eosin and examined under a light microscope. Photomicrographs were also taken.

Inflammation was evaluated using two different methods when the histopathological examination was performed:

For the first inflammation score, sections were obtained systematically and randomly. The degree of inflammation in the perivascular area was then scored in a double-blinded manner by two independent pathologists as shown below [9]:

0: No inflammatory cells;
1: A few inflammatory cells;
2: Several inflammatory cells in the peripheral regions of the perivascular region;
3: Numerous inflammatory cells in the perivascular area.

The second inflammation score was designed based on the presence of values indicating inflammation during the histopathological examination: Polymorphonuclear leukocytes (PMNL): Present/Absent, Vascular congestion (VC): Present/Absent, Edema: Present/Absent

### *2.6. Statistical analysis*

Numerical values obtained from the groups were expressed as mean ± standard deviation. Numerical data obtained from biochemical analyses were assessed using one-way ANOVA and Tukey tests, and p-values <0.05 were regarded as significant. Data yielded by histopathological examinations were analyzed using the Kruskal-Wallis and the Fisher–Freeman–Halton tests, and p-values < 0.05 were regarded as significant. All statistical analyses were performed on IBM SPSS-20 software.

## 3. Results

### *3.1. Biochemical findings*

Serum IL-1β levels in the CLP group increased significantly compared to the healthy control group ($p<0.001$). In addition, serum IL-1β levels decreased significantly in the L100 and L200 groups compared to the CLP group ($p<0.001$). Although a numerical decrease was observed in serum IL-1β levels in L100 and L200 groups, the difference was not statistically significant ($p>0.05$) (Fig. 1).

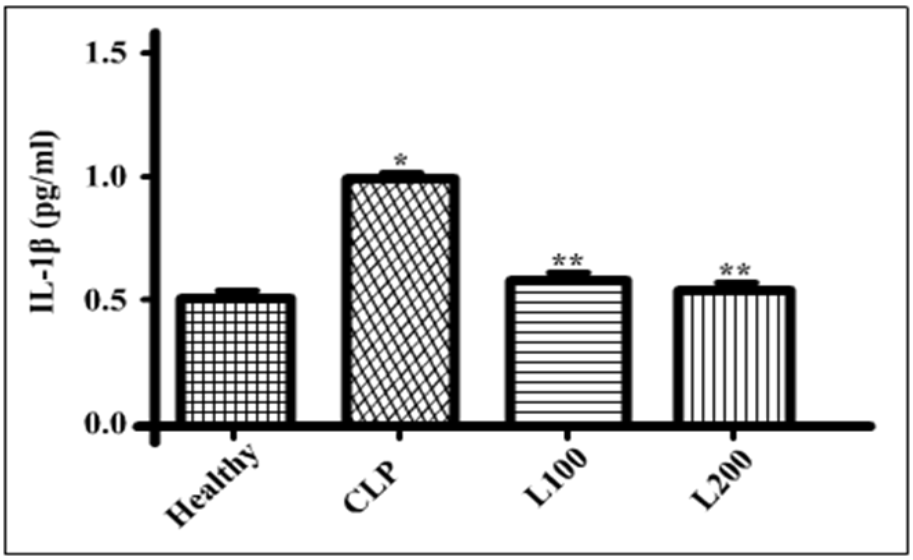


**Fig. 1.** Group healthy, Group ÇLP, Group L100, Group L200 IL-1β values in pg/ml.
* $p<0.001$ for the CLP group compared with the healthy group.
** $p<0.001$ for the CLP group compared with the L100 and L200 groups.

Serum IL-6 levels in the CLP group increased significantly compared to the healthy control group ($p<0.001$). The administration of both doses of lycopene in the L100 and L200 groups reduced serum IL-6 levels significantly compared to the CLP group ($p<0.001$). Serum IL-6 levels were also statistically significantly lower in the L200 group compared to the L100 group ($p<0.01$) (Fig. 2).

### *3.2. Histopathological findings*

Light microscopic examination revealed that pulmonary tissues from the rats in the healthy control group were within physiological limits: no inflammation, edema, nor congestion was observed (Fig. 3a). However, marked interstitial expansion and inflammation, diffuse conges-

tion, and edema were observed in the CLP group (Fig. 3b). The degree of Inflammation and congestion decreased while edema improved in the L100 group compared to the CLP group (Fig. 3c). Furthermore, we observed that the pulmonary tissue from the L200 group exhibited a morphology close to that of the healthy controls (Fig. 3d).

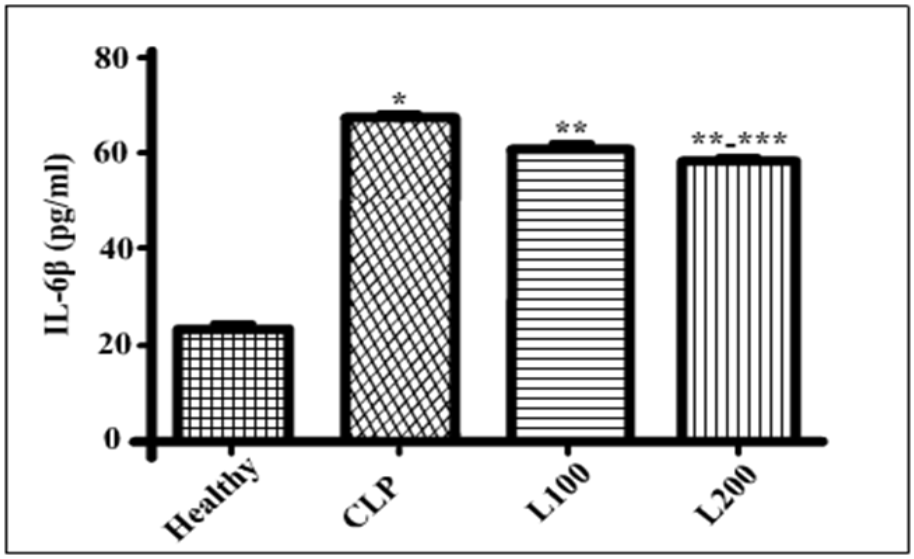


**Fig. 2.** Group healthy, Group CLP, Group L100, Group L200 IL-6 values in pg/ml.
* p<0.001 for the CLP group compared with the healthy group.
** p<0.001 for the CLP group compared with the L100 and L200 groups.
*** p<0.001 for the L200 group compared with the L100 group.

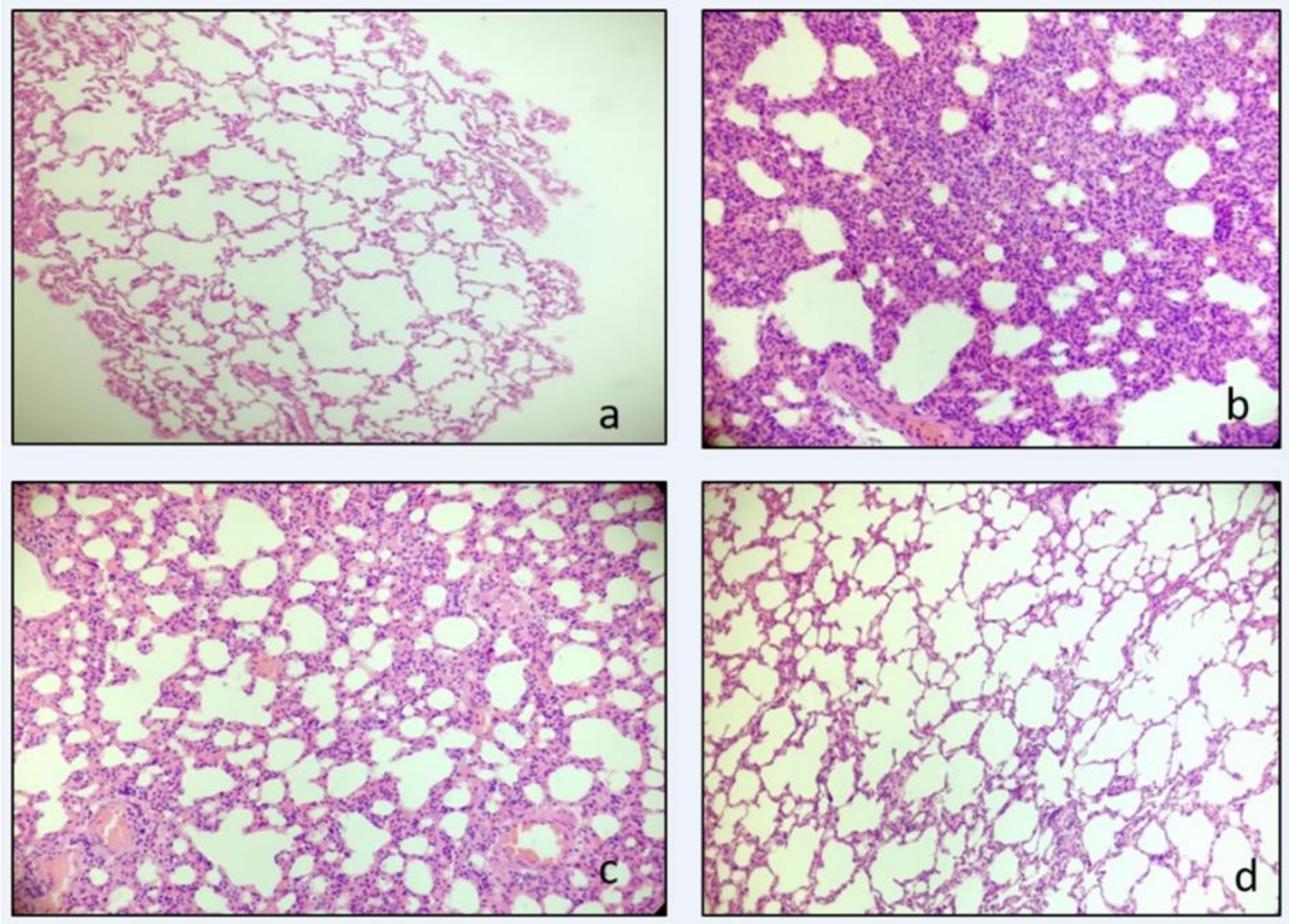


**Fig. 3.** Histopathological findings: (a) Healthy group; (b) CLP group; (c) L100 group; (d) L200 group.

### *3.3. Histopathological changes in lung tissues*

Histopathological inflammation scores in the study groups were produced for PMNL, VC, and edema (Table 1). We found that the degree of inflammation in the CLP group increased compared to the healthy control group, while it decreased in the L100 group compared to the CLP group and decreased more markedly in the L200 group compared to the CLP group.

Statistical analysis was performed using the Kruskal-Wallis test with the assumption that the variables were gradually increasing or decreasing ordinal variables. Analyzed in terms of PMNL, VC, and edema, the degree of inflammation in the CLP group increased significantly compared to the healthy control group ($p<0.001$). Assessed in terms of PMNL, VC, and edema, the degree of inflammation in the L200 group was significantly lower than in the CLP group ($p<0.001$). Again, assessed in terms of PMNL, VC, and edema, the degree of inflammation was also lower in the L100 group than in the CLP group, although the difference was not statistically significant ($p>0.05$). Similarly, although a numerical decrease in the degree of inflammation was observed in the L200 group compared to the L100 group, the difference was not statistically significant ($p>0.05$) (Table 2).

**Table 1.** A comparison of graded inflammation findings in lung tissue among the study groups.

| | | Healthy group (n=6) | CLP group (n=6) | L100 group (n=6) | L200 group (n=6) |
|---|---|---|---|---|---|
| PMNL | 0 | 3 (50%) | 0 (0%) | 0 (0%) | 1 (16.7%) |
| | 1 | 3 (50%) | 0 (0%) | 3 (50%) | 5 (83.3%) |
| | 2 | 0 (0%) | 0 (0%) | 3 (50%) | 0 (0%) |
| | 3 | 0 (0%) | 6 (100%) [a] | 0 (0%) | 0 (0%) [b] |
| VC | 0 | 2 (33.3%) | 0 (0%) | 0 (0%) | 5 (83.3%) |
| | 1 | 4 (66.7%) | 0 (0%) | 5 (83.3%) | 1 (16.7%) |
| | 2 | 0 (0%) | 2 (33.3%) | 1 (%16.7) | 0 (0%) |
| | 3 | 0 (0%) | 4 (66.7%) [a] | 0 (0%) | 0 (0%) [b] |
| Edema | 0 | 5 (83.3%) | 0 (0%) | 2 (33.3%) | 6 (100%) |
| | 1 | 1 (16.7%) | 0 (0%) | 4 (66.7%) | 0 (0%) |
| | 2 | 0 (0%) | 6 (100%) [a] | 0 (0%) | 0 (0%) [b] |

All data are expressed as number (percentage).
Kruskal Wallis test
CLP: Cecum ligation and perforation; PMNL: Polymorphonuclear leukocyte; VC: Vascular congestion.
[a] $p<0.001$ for the CLP group compared with the healthy groups.
[b] $p<0.001$ for the CLP group compared with the L200 groups.

**Table 2.** Comparison of graded inflammation findings in lung tissue among the groups.

| | | Healthy group (n=6) | CLP group (n=6) | L100 group (n=6) | L200 group (n=6) |
|---|---|---|---|---|---|
| PMNL | Median | 0.50 (0-1) | 3.00 (3-3) [a] | 1.50 (1-2) | 1.00 (0-1) [a] |
| VC | Median | 1.00 (0-1) | 3.00 (2-3) [b] | 1.00 (1-2) | 0.00 (0-1) [b] |
| Edema | Median | 0.00 (0-1) | 2.00 (2-2) [c] | 1.00 (0-1) | 0.00 (0-0) [c] |

Results were presented as mean ± standard deviation.
Kruskal Wallis test
CLP: Cecum ligation and perforation; PMNL: Polymorphonuclear leukocyte; VC: Vascular congestion.
[a] $p < 0.001$ for the CLP group compared with the healthy and L200 groups.
[b] $p < 0.001$ for the CLP group compared with the healthy and L200 groups.
[c] $p < 0.001$ for the CLP group compared with the healthy and L200 groups.

No statistically significant difference was observed between the groups when the presence or absence of PMNL in the lung tissues was used as a marker of inflammation ($p>0.05$). When the presence or absence of VC was evaluated as a marker of inflammation in the study groups, a significant decrease in inflammation was observed in the L200 group compared to the CLP group ($p<0.001$). VC was also significantly lower in the L200 group compared to the L100 group ($p<0.001$). When the presence or absence of edema was used as a marker of inflammation, a significant increase in edema was observed in the CLP group compared to the healthy control group ($p<0.001$). In addition, edema decreased in the L100 group compared to the CLP group, but this was not statistically significant ($p>0.05$). However, edema decreased significantly in the L200 group compared to the CLP group ($p<0.001$) (Table 3).

**Table 3.** A comparison of inflammation findings in lung tissue among the groups.

| | | Healthy group (n=6) | CLP group (n=6) | L100 group (n=6) | L200 group (n=6) |
|---|---|---|---|---|---|
| PMNL | (Yes/No) | 3/3 | 0/6 | 0/6 | 1/5 |
| VC | (Yes/No) | 2/4 | 0/6 [a] | 0/6 [b] | 5/1 |
| Edema | (Yes/No) | 5/1 [c] | 0/6 [a] | 2/4 | 6/0 |

Results were presented as number.
Fisher–Freeman–Halton test
CLP: Cecum ligation and perforation; PMNL: Polymorphonuclear leukocyte; VC: Vascular congestion.
[a] $p<0.001$ for the CLP group-L-200 group
[b] $p<0.001$ for the L100 group -L200 group
[c] $p<0.001$ for the healthy group-CLP group

## 4. Discussion

In our study, IL-1β and IL-6 levels were significantly decreased in both lycopene groups compared to the cecal ligation perforation group. When we look at our study in terms of histopathological findings, inflammation findings were decreased in both lycopene groups compared to the cecal ligation perforation group. A statistically significant decrease in inflammation was found in the L 200 group compared to the other groups.

Despite the variation in the incidence of sepsis and septic shock in the last 10 years, significant reductions have been observed since consensus decisions have been adopted for the treatment of severe sepsis in patients presenting to intensive care, leading to lower mortality rates. The reasons for this include early diagnosis, more conscious emergency treatment, and earlier initiation of antibiotic therapy [10]. However, there is still no reliable and specific parameter that can be used to promptly identify septic patients [11].

Models frequently employed for inducing experimental sepsis include intravascular lipopolysaccharide injection, induction of peritonitis by applying feces or bacteria into the peritoneal cavity, abscess creation with infected material, opening an intestinal segment, ascending colon stent peritonitis, and CLP [12]. CLP, a simple model that can be applied in clinical settings and can be used in all animal species to induce intra abdominal sepsis, has become a widely employed method in experimental studies. We, therefore, employed a CLP sepsis model in the present study.

In polymicrobial sepsis, cytokines such as IL-1β, IL-6, and TNF-α are released from intestinal epithelial cells. These cytokines have been proved to play an important role in the inflammatory response [13,14]. An increase in IL-6 levels has been identified as a marker of poor prognosis and linked to severe inflammatory complications [15]. Parameters such as IL 1β and IL-6 were therefore investigated in animals with CLP-induced sepsis in the present study. Several studies have reported significant increase in IL-1β, IL-6, and TNF-α levels due to the inflammatory response in induced sepsis models [15]. This is consistent with the findings of the present research and supports the model used to induce sepsis. Similar to previous literature, we found significantly higher IL-1β and IL-6 levels in the sepsis group than in the control group. Thus, we believe that IL-1β and IL-6 values can represent important parameters in the treatment of sepsis [16,17].

The present study employed lycopene, a hydrocarbon with known antioxidant, anticarcinogenic, and anti-inflammatory effects, and hypothesized that it might be beneficial in the treatment of sepsis. While our scan of the literature revealed that the antioxidant and anticarcinogenic effects of lycopene have been widely studied, there has been insufficient research on its anti-inflammatory effects in sepsis. We, therefore, investigated the anti inflammatory effect of lycopene in rats with induced sepsis. Lycopene suppresses inflammation by reducing the synthesis of the proinflammatory molecules—prostaglandin, prostacyclin, thromboxane, and leukotriene, and regulating cyclooxygenase and lipo oxygenase activities [18].

There is a known interaction between oxidative stress and inflammation. Nuclear factor Kappa-B is one of the protein complexes that control transcription in DNA and it is co present with inhibitor factor Kappa-B, which is generally found in the passive form in cytoplasm and becomes activated when it separates from inhibitor factor kappa-B through phosphorylation. According to Huang et al., lycopene can act as an anti-inflammatory molecule by inhibiting the binding activity of nuclear factor Kappa-B [19].

Chung et al. [21] determined that smoking increased IL-1β levels in smokers' saliva and phlegm [20]. Simone et al. exposed macrophages to cigarette smoke and showed that the increase in IL-8 synthesis reached a level that is close to that of the control group approximately 3 h after lycopene treatment. The authors thus determined that oxidative stress and inflammation were suppressed as a result of lycopene treatment.

The anticarcinogenic effect of lycopene observed in animal studies may be associated with the antioxidant activity of lycopene, stimulation of gap junctions providing intercellular signaling, induction of detoxification enzymes, and cellular proliferation inhibition. Studies have shown that lycopene may protect lipids, nucleic acids, and proteins against oxidative stress that is capable of resulting in cancer, and it has been suggested as potentially useful in the treatment of cancer [22,23].

Research has also demonstrated that lycopene can reduce the effects of toxic agents when administered together. Jamshidzadeh et al. [24] investigated the effects of tomato extract on pulmonary, hepatic, and renal tox-

icity induced in rats with amiodarone, acetaminophen, and cyclosporine, respectively, and reported biological and histopathological improvement in the groups in which lycopene was administered together with the toxic substances. A review study published by Petyaev [25] reported that, in studies on chronic vascular diseases using various animal models, lycopene led to increased endothelial nitric oxide synthase activity, which returned nitric oxide levels to normal, and improved endothelial function, as well as the weakening of inflammatory damage and inhibition of cholesterol biosynthesis.

Lycopene has been shown to exhibit beneficial effects in models of hypertension and diabetes [26,27]. Hyperglycemia is an important clinical parameter in the pathogenesis of sepsis and develops due to various causes. The use of lycopene in rats with induced sepsis in the present study is, therefore, particularly valuable. The effect of lycopene on sepsis-related hyperglycemia may be a subject deserving of investigation.

Colitis is not yet fully understood. Genetic and environmental factors, micro-organisms or their antigens, and immune system disorders have been implicated in the etiopathogenesis of colitis [28]. Reifen et al. [29] studied colitis in rats following iron supplementation and showed that lycopene reduced oxidative stress and inflammation. They also observed that lycopene had an anti-inflammatory effect.

Lung tissue is one of the organs that is affected in cases of sepsis. Cadirci et al. [9] evaluated lung damage in rats with sepsis that is induced using a CLP model. Their histopathological examination showed significantly greater PMNL infiltration, VC, and edema in the sepsis group than in the other study groups. A study investigating the protective effect of lycopene in a lung disease model induced in rats with oleic acid showed less neutrophilic infiltration and perivascular and alveolar edema in the lycopene group [30]. Lung damage is one of the principal pathologies that develop in sepsis and the main cause of secondary Acute Respiratory Distress Syndrome. In the present study, we investigated pulmonary histopathology using lycopene in rats with induced sepsis and detected a positive anti-inflammatory effect after the treatment.

Hua et al. [31] investigated acute lung damage as a result of induced sepsis in rats. The changes detected after histopathological analysis of the septic lung included pulmonary edema, breakdown of pulmonary alveolar structures, and inflammatory cell infiltration.

Demir et al. [32] performed a histopathological examination of the lungs of rats with CLP induced sepsis and observed mononuclear cell infiltration in lung tissue, increased capillary permeability, alveolar edema, diffuse alveolar injury, and increased numbers of alveolar macrophages. In light of the studies cited above, which showed that the lung is affected in sepsis, we believe that lycopene administration can be used to prevent pulmonary inflammation in a sepsis model.

As limitations of our study; CRP, Procalcitonin, platelet and leukocyte values in the blood should not be checked and only the lung should be evaluated histopathologically. These include not examining tissues that can be easily affected by sepsis-related inflammation, such as the liver, brain and kidney. A more comprehensive study could be conducted by increasing the number of rats.

## 5. Conclusions

In this study documenting in terms of serum IL-1β and IL-6 levels and changes occurring in lung tissues in a CLP-induced model of sepsis in rats, we believe that the use of lycopene in sepsis will be beneficial. In addition, we found that the 200 mg/kg lycopene dosage exhibited more positive effects than a dosage of 100 mg/kg in the treatment of sepsis in our CLP-induced model.

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***Conflict of Interest***

*The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this manuscript.*

***Data Availability***

*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

***Ethics Approval and Consent to Participate***

*This study was approved by the ethics committee of Atatürk University. Animal experiments were carried out with the decision of the local ethics committee dated 27.12.2018, number 13, decision number 235. Written informed consent was obtained from the participants. All methods were performed in accordance with relevant guidelines and regulations.*

***Author Contributions***

***Sumeyra Zeren:*** *investigation, methodology, data curation, writing – original draft.*
***Ozgur Ozmen:*** *conceptualization, supervision, writing – review & editing, project administration.*
***Zekai Halici:*** *methodology, resources, pharmacological oversight.*
***Sare Sipal:*** *histopathological analysis, visualization.*
***Betul Gundogdu:*** *histopathological analysis, validation.*
***Kamber Kasali:*** *formal analysis, statistical analysis, software.*
***Nazim Dogan:*** *methodology, animal experimentation support.*
***Husnu Kursad:*** *data curation, writing – review & editing.*

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Research Article

# Effects on cardiopulmonary bypass duration and optic nerve sheath diameter changes

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## ABSTRACT

**Background:** Cardiopulmonary bypass (CPB) causes disruption of the blood-brain barrier and cerebral autoregulation for many reasons. The resulting cerebral edema causes an increase in intracranial pressure. Ultrasonographic optic nevre sheath diameter (ONSD) measurement is one of the non-invasive methods that provides information about intracranial pressure. Numerous studies have demonstrated a correlation between ONSD and intracranial pressure (ICP). We aimed to investigate ONSD changes during CPB and the relationship between these changes and CPB duration.

**Methods:** Twenty six patients aged between 18-75 years, with an ASA score of II or III, which underwent cardiac surgery with CPB are included to the study. ONSD measurements were made throughout surgery and data were recorded.

**Results:** ONSD values increased significantly at 45 and 90 min of CPB and end of the surgery compared to pre-CPB values for both eyes. There was no significant difference between 45 and 90 min. during CPB. A critical ONSD value was detected in 12 patients during CPB. No patient developed neurologic adverse events in the postoperative period.

**Conclusion:** ONSD increased during CPB regardless of duration. With the data obtained from our study, we cannot say that the increase in ONSD will be a predictor of postoperative neurological complications.

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## 1. Introduction

Extracorporeal circulation with Cardiopulmonary bypass (CPB) are utilized during most cardiac surgical interventions. Despite advances in anaesthesia and surgical techniques, CPB still has the potential to cause various complications in certain tissues and organ functions of the body. Such complications can lead to undesirable neurologic events [1]. Hypoxic ischemic events, embolism, changes in the blood-brain barrier, and increased intracranial pressure (ICP) are among the causes of postoperative adverse neurologic outcomes [2,3]. CPB may contribute to ischemia-reperfusion injury and the release of inflammatory substances, disruption of the integrity of the blood-brain barrier and increase in ICP [4]. Some studies have reported that prolonged CPB duration may

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damage the blood-brain barrier and extended duration of CPB alongside cross-clamp (CC) times increases brain damage [5].

The first sign of increased ICP is optic disc enlargement. However, ophthalmoscopic evaluation may not be feasible in all patients [6].

The sheath enveloping the optic nerve maintains continuity with the dura mater and the subarachnoidal space filled with cerebrospinal fluid (CSF), forming a direct connection between the two compartments. Due to the extensible nature of the optic nerve sheath, CSF pressure changes in the diameter of the optic nerve sheath with fluctuations in the anterior retrobulbar compartment approximately 3 mm behind the globe [7]. The ultrasonographic evaluation of ONSD was first proposed in 1987 as a tool to measure ICP [8] .

Numerous studies have demonstrated a correlation between ONSD and ICP [9,10]. Its diagnostic accuracy has been studied in various patient groups [11,12]. Studies in cardiac surgery suggest a positive correlation between ONSD and the duration of extracorporeal circulation [13–16]. Elevated ONSD values are associated with a higher risk of adverse neurological outcomes postoperatively, particularly in patients with prolonged CPB durations. It has been proposed that ONSD measurement could serve as a predictive tool for such outcomes [14,15]. Conversely, Rivas-Rangel et al. [13] reported cases where increased ONSD was not accompanied by symptoms of elevated ICP. ONSD has also been suggested as a potential indicator for assessing intravascular volume status [16]. In another study, Kara et al. [14] highlighted its utility as part of intraoperative monitoring during coronary artery bypass grafting (CABG). However, several studies emphasize the need for further research with larger patient cohorts and extended follow-up periods to clarify the effects of CPB duration on ONSD and identify factors influencing ONSD variations [13,17].

Based on these findings, our primary aim was to investigate the ONSD changes during CPB and the relationship between these changes and CPB duration. Our secondary aim was to evaluate adverse neurological events, delayed awakening (the failure of the standard patient to open her eyes and to respond spontaneously to calls from people without any physical contact or stimulus within 2 hours after termination of anesthesia despite despite our routine anesthesia protocol, normothermia, and stable hematologic and biochemical parameters), hemiparesis, hemiplegia, slurred speech, agitation, or poor response to commands, extubation time, and length of stay in the ICU within the first 24 hours.

## 2. Materials and Methods

After Kocaeli University ethics committee approval (GOKAEK-2023/08.22) and informed consent of the patients were obtained, 26 patients, aged between 18–75 years, with ASA scores of II-III, who were planned to undergo CPB-guided open heart surgery, were included in this prospective observational study. Patients with a known ophthalmologic disease, a history of ophthalmologic surgery, known neurologic disease, previous cerebrovascular accident, and intracranial pathology were excluded. Upon arrival at the operating room, patients were administered oxygen at a rate of 5 L/min via a face mask. Preoperative monitoring included electrocardiography (ECG), peripheral oxygen saturation ($SpO_2$), regional cerebral oximetry ($rSO_2$), and noninvasive blood pressure measurements. Midazolam at a volume of 0.02 mg/kg and fentanyl at 1 μg/kg intravenously (iv) was administered, followed by local anaesthesia with lidocaine, and radial artery cannulation was performed in the non-dominant hand. Anaesthesia induction was performed with 5–7 μg/kg fentanyl, 2 mg/kg thiopental (if necessary, an additional 1 mg/kg volume was administered until the eyelash reflex disappeared), and 0.8 mg/kg rocuronium. Patients were intubated after preoxygenation and controlled mechanical ventilation was started with a tidal volume of 8 ml/kg according to predicted body weight. Mechanical ventilation parameters were set as I: E ratio 1:2, plateau time 20% of the inspiratory time (Ti), PEEP 5 cm $H_2O$. The respiratory rate (RR) was initially started as 10/min. RF was adjusted so that the end-tidal carbon dioxide ($EtCO_2$) values were between 35–40 mmHg. Oxygen concentration was increased when $SpO_2$ dropped below 97% as in our routine clinical practice.

Following anaesthesia induction, a central venous pressure (CVP) catheter was inserted, preferably into the right internal jugular vein. A rectal and nasopharyngeal temperature measurement probes and a urinary catheter were placed. Anesthesia was maintained using a mixture of 40% oxygen and 60% air and desflurane inhalation at a 0.7–1.0 minimum alveolar concentration (MAC). Continuous remifentanil infusion at a rate of 0.1-0.4 μg/kg/min was administered before and after CPB, adjusting the dosage based on the patient's hemodynamic response. In the event of hypotension Mean arterial pressure (MAP) <65 mmHg for ≥1 minute, the following steps are taken in sequence until target blood pressure is achieved: placing the patient in the Trendelenburg position, infusing 250 mL of colloid administering a 5–10 mg intravenous bolus of ephedrine. In hypertension (more than 20% increase in systolic arterial pressure compared to baseline), iv. Bolus fentanyl, and for bradycardia heart rate (HR) <50 beats/min, 0.5 mg iv atropine administration was planned. Following systemic heparinisation and the completion of arterial and venous cannulations, CPB was initiated when the activated clotting time (ACT) level exceeded 480 seconds. Anesthesia was maintained by a desflurane vaporizer integrated into the CPB circuit. A flow rate of 2.2–2.4 L/min/$m^2$ and perfusion pressure of 60–80 mmHg were maintained during CPB.

Myocardial protection was achieved through the application of hyperkalemic blood cardioplegia. The lungs were not ventilated during the CPB and they were connected to the Bain circuit with a baseline oxygen flow of 200 ml/min. Mild to moderate systemic hypothermia was applied during CPB, and the patient was rewarmed after the last distal anastomosis was completed. Midazolam (0.03 mg/kg) and rocuronium bromide (0.15 mg/kg) were given at the beginning of CPB and during rewarming. Throughout the surgical procedure, an additional in-

travenous bolus of fentanyl (3 μg/kg) was administered during periods when sympathetic stimuli were most pronounced, and the avoidance of hypertension and tachycardia was imperative (skin incision, sternotomy, aortic cannulation, initiation and termination of CPB, rewarming, during and after CPB and skin closure). Following weaning from CPB, the cannulas were removed, and heparin was neutralized with protamine. Fluid, blood, and blood product, inotropic and vasopressor support were determined according to our routine clinical practice based on MAP, CVP, lactate values, arterial and venous oxygen pressure, $rSO_2$ and hematocrit values, and urine output. At the end of the surgery, the patients were transferred to the cardiovascular surgery intensive care unit. Standard postoperative analgesia protocol was applied to all patients. Patients were extubated when appropriate conditions were met.

### *2.1. ONSD measurement*

Studies have suggested that novice ultrasound users can become proficient in scanning in as little as 25 examinations, while an experienced sonographer can become proficient in as few as ten scans [18]. Before starting our study, the researcher who will measure ONSD completed the learning process in 25 patients with a radiologist. ONSD measurement was performed by the anaesthesia trainee, who completed the training process in the presence of an expert radiologist (NY). The patient's eyes were closed and covered with a bio-occlusive dressing (Tegaderm®; 3M™ Healthcare). A thick layer of ultrasound gel was applied over Tegaderm®. A linear array ultrasound transducer was gently placed on the gel over the eye. The position of the probe was adjusted to obtain appropriate images. Bilateral ONSD was measured 3 mm posterior to the papilla. ONSD measurements were taken at four-time points: initiation of CPB ($T_1$), at 45 minutes into CPB ($T_2$), at 90 minutes into CPB ($T_3$), and end of surgery ($T_4$). MAP, arterial blood gas parameters (pH, $paO_2$, $pCO_2$, $SaO_2$, $ScvO_2$, lactate, haemoglobin, and hematocrit), $rSO_2$, body temperature and end-tidal desflurane ($End\text{-}Tidal_{Desf}$) concentrations were measured at ONSD measurement times. In addition, HR, RF, expired tidal volume (TV Eksp), peak inspiratory pressure (PIP), plateau pressure (PP), dynamic compliance (Cdyn), and CVP values were also recorded at times outside of CPB.

Vivek et al. [15] reported that if the maximum ONSD recorded during CPB exceeded 5.5 mm, the probability of adverse postoperative neurologic outcome was higher. Inspired by this study, an ONSD value greater than 5.5 mm in either the right or left eye was considered critical.

Adverse neurologic event was defined as delayed awakening (the failure of the standard patient to open her eyes and to respond spontaneously to calls from people without any physical contact or stimulus within 2 hours after termination of anesthesia despite despite our routine anesthesia protocol, normothermia, and stable hematologic and biochemical parameters), hemiparesis, hemiplegia, slurred speech, agitation, or poor response to commands. The patients were evaluated by an anesthesia assistant who was not involved in anesthesia management for 24 hours postoperatively.

### *2.2. Statistical analysis*

Based on the ONSD measurements obtained from a 12-person pilot study at pre-CPB ($T_1$) and 90 minutes during CPB ($T_3$), a sample size of 23 was calculated using the G*Power 3.1.9.4 program for $\alpha$=0.05 and Power (1-$\beta$)=0.95. Considering a predicted 10% data loss, 26 individuals were planned for the study. Statistical analysis was conducted using IBM SPSS 29.0 (IBM Corp., Armonk, NY, USA). Normal distribution was assessed using the Shapiro-Wilk test. Normally distributed variables were presented as mean ± standard deviation, non- normally distributed variables as median (25th–75th percentile), and categorical variables as frequency (percentage). Friedman's two-way ANOVA and Wilcoxon signed-rank tests were used for dependent group comparisons. Dunn's test was used for the multiple comparisons. A p value < 0.05 was considered statistically significant.

## 3. Results

In our study, a total of 26 patients were included initially. However, one patient had to be excluded from the study due to the requirement for extracorporeal membrane oxygenation support at the end of surgery, the data of 25 patients were analyzed (Table 1).

Compared to pre-CPB values, ONSD increased significantly in both eyes at 45th and 90th minutes of CPB (for the right eye; p=0.037, p<0.001 and for the left eye; p=0.007, p=0.001, respectively). ONSD values decreased at the end of surgery but were still significantly higher than pre-CPB values (for the right eye; p=0.007, for the left eye; p=0.009). ONSD values showed similar changes at 45th and 90th minutes of CPB (for the right eye; p=0.424, for the left eye; p=1.000). Changes in ONSD during CPB are shown in Figs. 1 and 2. With the introduction of CPB, significant changes were found not only in ONSD but also in MAP, body temparature, Hb, Htc, $rSO_2$, pH, $paO_2$, $SaO_2$, $ScvO_2$, lactate values and inhaled desflurane concentration compared to pre-CPB values (Table 2). We found that 12 patients had ONSD measurements above this critical value, critical ONSD values were determined only during CPB. In the postoperative period, no adverse neurological events developed in any patient.

## 4. Discussion

The data of this study showed that ONSD increased significantly from the beginning of CPB and independently of the duration of CPB. At the end of surgery, ONSD decreased but was still significantly higher than pre-bypass data. No postoperative adverse neurologic events occurred in any patient, including 12 patients who exceeded the critical ONSD value.

In studies conducted in cardiac surgery, it has been reported that ONSD, which is accepted as a non-invasive measurement method of intracranial pressure, increases as the CPB duration increases [13,17]. The

blood-brain barrier is affected by body temperature, blood flow pattern, viscosity, $O_2$ and $CO_2$ pressure and cardiopulmonary bypass [19,20]. When the data in Table 2 are analyzed, it is seen that significant changes occur in many parameters and ONSD starting from the 45th minute of CPB and these changes continue throughout CPB. The downward trend in $T_4$ and the change in ONSD suggest that it is transient.

**Table 1.** Perioperative data of the patients.

| | |
|---|---|
| Age, year | 62.24 ± 9.87 |
| Weight, kg | 79.20 ± 8.65 |
| Gender, M/F, n (%) | 7 (28) / 18 (72) |
| ASA, II/III, n (%) | 13 (52) / 12 (48) |
| BMI ($kg/m^2$) | 26,90 ± 3,69 |
| Surgery, n (%)<br>CABG/Valve repair or replacement/Combined | 16 (64) / 7 (28) / 2 (8) |
| Comorbidity, n (%)<br>Hypertension/Respiratory/Diabetes, | 7 (28) / 11 (44) / 7 (28) |
| Carotid pathology, present/absent, n (%) | 2 (8) / 23 (92) |
| EF, % | 60.00 (45.00-60.00) |
| Fentanyl, mcq | 600.00 (575.00-700.00) |
| Muscle relaxant, mg | 90.00 (75.00-100.00) |
| CC duratiom, min | 78.00 (60.00-95.00) |
| CPB duration, min | 132.00 (111.00-146.00) |
| Cardioplegia, ml | 3000.00 (2000.00-4000.00) |
| Duration of anesthesia, hours | 6.00 (5.00-6.75) |
| End-surgical balance, ml | 1350.00 (848.00-1925.00) |
| Inotrope requirement, n (%)<br>None/single inotrope/two inotropes | 8 (32) / 5 (48) / 12 (20) |
| Blood and blood product requirement, yes/no, n (%) | 14 (56) / 11 (44) |
| Ephedrine requirement, yes/no, n (%) | 5 (20) / 20 (80) |
| Atropine,requirement yes/no, n (%) | 0/25 |
| Extubation time, hours | 5.00 (4.00-8.00) |
| Duration of intensive care, hours | 48.00 (48.00-60.00) |
| ONSD >5.5 mm, n (%) | 12 (48) |
| $ONSD_{right,\ meam}$, mm | 4.70 |
| $ONSD_{left,\ meam}$, mm | 5.10 |

Values are given as n(%), median (25–75) percentile or mean±SS

ASA: American Society of Anesthesiologists; EF: Ejection Fraction; ONSD: Optic Nerve Sheath Diameter; CABG: Coronary artery bypass graft.

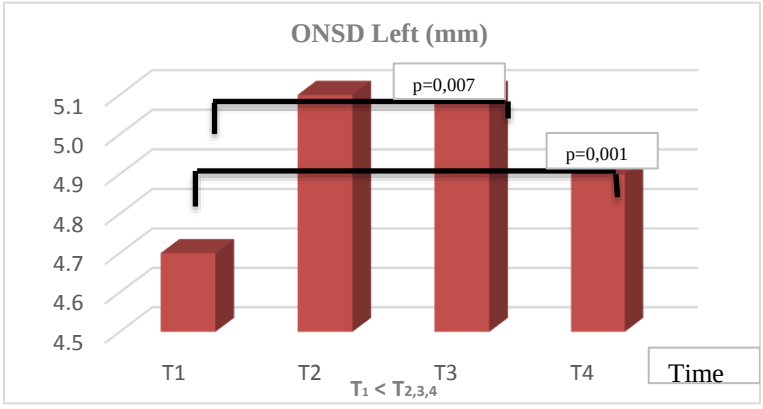


**Fig. 1.** Changes in ONSD during CPB-Left.

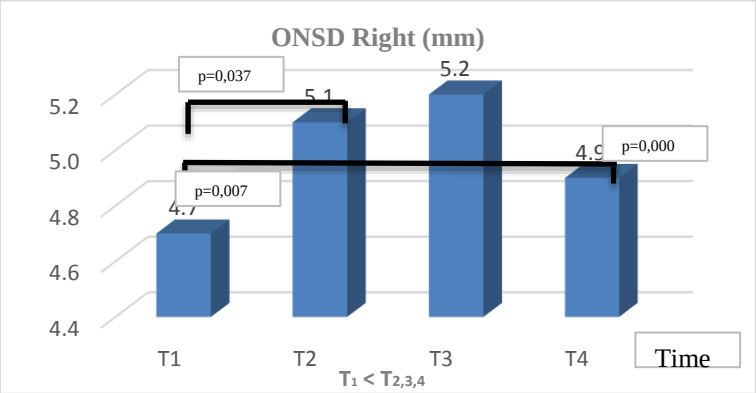


**Fig. 2.** Changes in ONSD during CPB-Right.

**Table 2.** Intraoperative changes seen during CPB compared to before and after CPB.

| | $T_1$ | $T_2$ | $T_3$ | $T_4$ | p | Pairwise comparison |
|---|---|---|---|---|---|---|
| $ONSD_{right}$, mm | 4.7 (4.3-5.0) | 5.1(4.75-5.35) | 5.2(4.85-5.5) | 4.9(4.6-5.2) | <0.001[a] | $T_1 < T_{2,3,4}$ |
| $ONSD_{left}$, mm | 4.7(4.4-5.05) | 5.1(4.8-5.3) | 5.1(4.8-5.4) | 5.0(4.7-5.2) | <0.001[a] | $T_1 < T_{2,3,4}$ |
| MAP, mmHg | 63.0(60.0-68.0) | 57.0(54.0-73.0) | 65.0(60.0-70.0) | 73.0(68.0-78.5) | <0.001[a] | $T_1 > T_2$ $T_4 > T_{1,3}$ $T_3 > T_2$ |
| Body temperature, °C | 36.2(35.9-36.65) | 33.0(32.0-33.0) | 32.0(32.0-33.0) | 36.2(35.9-36.7) | <0.001[a] | $T_1 > T_{2,3}$ $T_4 > T_{2,3}$ |
| Hb, g/dL | 12.7(11.1-13.2) | 8.9(7.55-9.8) | 9.0(8.2-10.1) | 9.7(9.2-10.4) | <0.001[a] | $T_1 > T_{2,3,4}$ $T_4 > T_2$ |
| Htc, % | 37.5(32.75-42.0) | 27.0(23.6-29.9) | 27.7(25.65-31.15) | 30.0(28.1-32.75) | <0.001[a] | $T_1 > T_{2,3,4}$ $T_4 > T_2$ |
| $rSO_{2\text{-right}}$, % | 85.0(78.5-94.0) | 78.0(70.0-87.5) | 80.0(71.0-86.5) | 81.0(72.5-85.5) | 0.002[a] | $T_1 > T_{2,3,4}$ |
| $rSO_{2\text{-left}}$, % | 84.0(80.5-88.5) | 81.0(70.5-85.5) | 78.0(71.5-86.0) | 81.0(73.0-84.5) | <0.001[a] | $T_1 > T_{2,3,4}$ |
| ph | 7.41(7.39-7.44) | 7.36(7.34-7.38) | 7.35(7.32-7.38) | 7.36(7.31-7.39) | <0.001[a] | $T_1 > T_{2,3,4}$ |
| Lactate, mol/L | 1.0(0.8-1.3) | 1.5(1.15-1.8) | 1.9(1.35-2.45) | 2.2(1.5-3.95) | <0.001[a] | $T_1 < T_{3,4}$ $T_2 < T_{3,4}$ |
| $PaO_2$, mmHg | 141.0(96.7-170.5) | 302.0(246.0-328.0) | 296.0(249.50-330.0) | 103.0(78.75-158.5) | <0.001[a] | $T_1 < T_{2,3}$ $T_4 < T_{2,3}$ |
| $PaCO_2$, mmHg | 36.0(34.70-37.75) | 37.9(35.0-41.45) | 39.0(37.2-41.25) | 38.0(35.65-39.75) | 0.003[a] | $T_1 < T_3$ |
| $SaO_2$, % | 98.0(97.0-99.0) | 99.0(99.0-99.35) | 99.0(99.0-99.5) | 98.0(96.75-99.0) | <0.001[a] | $T_1 < T_{2,3}$ $T_4 < T_{2,3}$ |
| $ScvO_2$, % | 76.0(71.50-79.0) | 84.2(80.3-86.5) | 80.0(74.5-86.5) | 77.0(70.6-82.55) | <0.001[a] | $T_1 < T_{2,3}$ $T_4 < T_2$ |
| $EndTidal_{Desf}$, % | 5.00(4.00-5.00) | 4.00(3.50-4.00) | 4.00(3.00-4.00) | 5.00(4.00-5.00) | <0.001[a] | $T_1 > T_{2,3}$ $T_4 > T_{2,3}$ |
| HR, beat/min | 73.0(64.5-81.5) | - | - | 89(82.5-98.5) | 0.002[b] | |
| RF, breath/min | 12.0(11.0-12.0) | - | - | 12.0(12.0-14.0) | 0.008[b] | |
| TVexpirium, ml | 560.0(505.0-606.5) | - | | 550.0(495.5-615.0) | 0.820[b] | |
| PIP, $cmH_20$ | 17.0(15.0-20.5) | - | - | 19.0(16.0-21.5) | 0.272[b] | |
| PP, $cmH_20$ | 15.0(13.0-18.0) | - | - | 16.0(13.5-18.0) | 0.822[b] | |
| Cdyn, $l/cmH_20$ | 54.0(45.0-71.9) | - | - | 52.5(40.0-65.5) | 0.484[b] | |
| CVP, mmHg | 12.0(11.0-13.5) | - | - | 12.0(10.5-15.5) | 0.084[b] | |

Values are given as median (25–75) percentile.

a: Friedmen's two way ANOVA with Dunn's test; b: Wilcoxon Signed rank test.

ONSD: Optic nerve sheath diameter; MAP: Mean arterial pressure; $rSO_2$: Regional serebral oxygen saturation; HR: Heart rate; RF: Respiratory frequency; TV: Tidal volume; PIP: Peak inspiratuar pressure; PP: Plateau pressure; Cdyn: Dynamic compliance; CVP: Central venous pressure.

$T_1$: 10 min before initiation of CPB; $T_2$: 45th min of CPB; $T_3$: 90th min of CPB; $T_4$: End of surgery.

The parameters in Table 2 including MAP, body temperature, Hb and Htc, right and left $rSO_2$, $paO_2$, $SaO_2$, $ScvO_2$ and end-tidal desflurane levels show significant differences at the 45th and 90th minute of CPB. Each of these changes can cause fluctuations in cerebral perfusion and may lead to an increase in ONSD due to anatomical relationship [21,22]. Our findings do not support the idea that there is a positive correlation between ONSD and CPB duration reported in previous studies [13,16]. Several of the studies have reported that further research with larger patient populations and longer patient follow-up is needed to identify the effect of CPB and CPB duration on ONSD as well as to identify factors related to variations in ONSD [13,17].

The fact that ONSD did not continue to increase at $T_3$ and showed a decreasing trend at $T_4$ suggests that ONSD, and thus ICP, is only associated with acute exacerbation of CPB. We may be mistaken if we think that increases in ONSD are only a reflection of changes in cerebral perfusion caused by CPB. Because in an animal study, hemodilution changes in the optic nerve and intraoperative ischemic damage were found to lead to optic neuropathy and optic nerve damage [23].

Hypotension, arrhythmia, hypercoagulopathy and hypothermia during surgery and CPB, decreased blood flow with hypothermia, prolonged CPB times and use of vasopressor agents increase ischemia in the optic area [24,25]. It has been reported that changes in ONSD may also be detected in neuropathies involving the optic nerve [26–28] .Further studies are needed to differentiate whether the changes in ONSD during CPB are really a reflection of impaired cerebral perfusion or whether it is really a damage to the optic nerve.

Previous systematic reviews and meta-analyses have demonstrated that an ONSD value exceeding 5.00 to 5.70 mm is associated with an ICP value above 20 mmHg [29,30]. Vivek et al. [15] investigated the relationship between postoperative neurological complications, ONSD, and CPB durations and stated that if the maximum ONSD recorded during CPB exceeded 5.5 mm, there was a higher likelihood of postoperative adverse neurological outcomes. However, 33 of 44 patients with no adverse neurological outcome had ONSD above 5.5 mm. The authors stated that a maximum ONSD anytime during CPB has a high sensitivity, specificity, diagnostic accuracy, as well as predictive value of negative test [15]. In the study of Taşkın et al. [17] no cut-off value of ONSD and no adverse neurological outcomes were mentioned. Kara et al. [14] reported that no critical ONSD value was obtained in any patient, and no perioperative neurological complications were observed. The authors stated that during extracorporeal circulation, ultrasound-guided ONSD measurement is an easy, inexpensive, and low-complication method that can be used as a part of monitoring during cardiac surgery and may be a predictor of increased ICP [14,17].

In a study conducted in pediatric patients undergoing congenital cardiac surgery, a positive correlation was found between ONSD values measured at 24 hours postoperatively and the duration of CPB. However, ONSD increase was also observed in patients without signs of increased ICP in this study. The authors stated that these results are insufficient to draw definitive conclusions, and more studies are needed to determine the factors that cause ONSD change [13]. In accordance with Rivas-Rangel et al. [13] , the factors responsible for ONSD change caused by CPB are not elucidated sufficiently, and more comprehensive studies are required.

In our study there was no adverse neurologic event in any patient at 24 hours postoperative follow-up. Based on these data from our study, we do not think that there is a positive association between the critical ONSD value and adverse neurologic events and that the critical ONSD value may be a predictor of adverse neurologic events. However, in our study, ONSD values at 45 and 90 minutes of CPB were found to be similar and therefore our primary hypothesis could not be confirmed. When we compare the results of studies conducted on this subject, both similarities and differences can be found due to methodological differences. For example, in the study by Taşkın et al. [17] , the ONSD was measured just before the start of the CPB, and at the 30th minute, 60th minute and 90th minute of the CPB. During the CPB, ONSD and nICPONSD values increased over time, and there was a statistical difference between the 0th, 30th, 60th and 90th minutes. All comparisons were made with the initial values ($T_0$). In our study, when we compared with the pre-bypass values, a significant increase was found during the CPB period, but when the changes were examined according to the CPB period, no significant difference was found between the 45th and 90th minutes of the CPB.

In the study by Kara et al. [14]. ONSD measurements were performed immediately before surgery, after intubation, 15 minutes after cross-clamping, after removal of the cross-clamping, and at the end of the operation and mean ONSD values at all stages during surgery were statistically significantly higher than the mean basal measurement.

Our study was performed with a small number of patients and that preoperative and postoperative ONSD measurements were not performed may be considered among the limitations of our study. The fact that the follow-up of postoperative adverse neurologic events was not limited to 24 hours and the patient was not followed up for neurologic complications in the late postoperative period is another limitation.

Patients cannot be limited to a 24 hour observation period for postoperative undesirable neurological complications; therefore, follow-up may be required in the later postoperative period as well. In our pilot study, we did not include pre-anesthesia ONSD measurement in the methodology, as performing this measurement in two awake patients caused discomfort. This may represent another limitation of our study.

## 5. Conclusions

CPB during open-heart surgery elevates ONSD independently of duration. However, our data do not support ONSD as a reliable predictor of postoperative neurologic complications. Further research is warranted to elucidate the multifactorial mechanisms underlying ONSD variability and its clinical implications.

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***Conflict of Interest***

*The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this manuscript.*

***Data Availability***

*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

***Ethics Approval and Consent to Participate***

*This study was approved by the ethics committee of Kocaeli University (approval number: GOKAEK-2023/08.22; date: 04.05.2023). Written informed consent was obtained from the participants and/or legal guardian(s) of the patients. All methods were performed in accordance with relevant guidelines and regulations. No violation of Helsinki Declaration was taken place during informed consent and data acquisition period.*

***Author Contributions***

***Tulay Cardakozu:*** *investigation, methodology, data curation, writing – original draft.*
***Nur Nazire Yucal:*** *conceptualization, supervision, formal analysis, writing – review & editing, project administration.*
***Ali Ahmet Arikan:*** *resources, validation, clinical support.*
***Sevim Cesur Okan:*** *methodology, visualization, writing – review & editing.*
***Oguz Omay:*** *surgical investigation, patient recruitment, resources.*

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Challenge Journal of Perioperative Medicine

Research Article

# The impact of vagal nerve stimulation from the lateral neck region on venous cannulation pain: A randomized controlled trial

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## ABSTRACT

**Background:** As the cranial nerve with the longest and widest distribution area of the body, the vagus nerve (N.Vagus) has both antinociceptive and neuromodulatory effects and plays a role in the regulation of the heart rate. The objective of this study is to investigate the impact of cold stimulation on vascular access discomfort and heart rate variability, specifically by separately stimulating the N. Vagus nerve on both the right and left sides of the neck thereby assessing any lateralization effect.

**Methods:** 140 patients, ranging in age from 18 to 75, were randomly assigned to one of two groups: Group Left (Group L) or Group Right (Group R). Following cold application to the left lateral neck region of Group L and the right lateral neck region of Group R, venous cannulation was performed. Prior to, following, and subsequent to vascular access, the heart rate, noninvasive blood pressure, oxygen saturation, and numeric pain scale (NRS) values for venous cannulation pain of the patients were documented.

**Results:** Average heart rates and average heart rates after cannulation were considerably lower in both groups after vagal stimulation ($p<0.05$). No significant difference was observed when comparing the average heart rate values for each time period in Group L and Group R, including the mean heart rate values before vagal stimulation, after vagal stimulation, and after vascular access ($p>0.05$). The mean heart rate change percentages before and after vagal stimulation were 7±5.8% and 7.1±7.0% in group L and group R respectively, suggesting that heart rate variability was greater in Group R, although this difference was not statistically significant ($p>0.05$). NRS values were found to be 2.64±1.28 in Group L and 2.85±1.62 in Group R, with no significant difference ($p>0.05$).

**Conclusion:** While heart rate variability exhibited more prominence on the right side, the difference was not statistically significant. Analyzing the analgesic impact revealed no discernible difference between the analgesic effects of stimulation from the right and left sides.

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## 1. Introduction

The vagus nerve (N. Vagus) extending from the brainstem to the final third of the large intestine, possesses the most extensive distribution area of and is the longest cranial nerve [1,2]. Numerous systems are regulated by N. Vagus, such as the respiratory, endocrine, immune, and autonomic systems. It originates on the lateral aspect of the medulla, traverses the jugular foramen to exit the cranium, and proceeds towards the thorax, abdomen, and neck [2,3]. The vagus nerve comprises of motor, sensory, and parasympathetic fibers, with 80% of these fibers being afferent and 20% efferent. A, B, and C fibers possess distinct physiological functions. Animal studies

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have demonstrated that vagal afferent C fibers are antinociceptive [2–4]. Originating in the brainstem, the vagal system extends throughout the thoracic and abdominal organs through descending branches from both sides of the anterior cervical area. The anatomical extent of the right and left branches of the N. Vagus the primary neuronal element of the parasympathetic system, varies along its trajectory. There is significant data indicating that vagal stimulation has an impact on both pain perception and gastrointestinal motility [3]. Vagal activation is recognized to contribute to pain regulation by reducing inflammation and modulating neuronal activity in pain pathways [2]. The cymba conchae region of the ear contains an afferent branch of the Vagus nerve, while the neck region is densely populated with its cervical branch [5]. These areas are used to stimulate the N. Vagus different sides and for different purposes [6].

Aside from its application as a neuromodulatory treatment for vagal stimulation resistant epilepsy and depression, it's efficacy has been demonstrated in the treatment of headache, tinnitus, atrial fibrillation, schizophrenia, and different forms of pain [2,7,8]. For millennia, Eastern medicine has harnessed the pain-relieving properties of ear acupuncture [9]. Various methods of stimulating the vagus nerve have been developed, including invasive techniques as well as non-invasive approaches such as transcutaneous, transcervical, and transauricular stimulation devices [2,6,10].

Stimulating the vagal nerve activates the baroreceptor reflex arc. Consequent release of 'substance P' resembling molecules are thought to be responsible for antinociceptive properties [11–13]. Applying cold to the neck area triggers the baroreceptor reflex arc by stimulating the vagus nerve, which activates the parasympathetic system leading to pain-relieving effects [12,14].

Prior to any anesthetic surgery, it is imperative to establish vascular access, which is frequently performed by anesthesiologists both inside and outside the operating room. Venous cannulation is a procedure that causes mild pain and discomfort for patients, leading to an increase in patient stress [15]. Numerous approaches have been explored to alleviate the discomfort associated with venous cannulation. Various techniques, including injecting local anesthetic into the affected area, using topical anesthetic, applying cold, and using a vibrating buzzy device, have been employed to alleviate the patient's pain and to divert their attention. The use of local anesthetic only decreases the physical aspect of pain, but the Valsalva technique, which stimulates the vagus nerve, has been shown to reduce both the physical and psychological aspects of pain [13]. Activation of the cardiopulmonary baroreceptor reflex arc or the sino-aortic baroreceptor reflex arc, along with the Valsalva maneuver, leads to antinociception while increased intrathoracic pressure caused by this maneuver results in a decrease in venous return, making the veins more visible and facilitating venous cannulation [16]. It is believed that the pain relieving effect of the vagus nerve in humans may be due to inhibition of pain signals in the central nervous system rather than through peripheral pain-relieving processes [14].

We previously discovered that the N. Vagus was activated, resulting in a decrease in heart rate and alleviation of vascular pain when ice was applied to the neck area. We believe that the application of cold to the neck area stimulates the baroreceptor reflex arc through vagal stimulation, thereby activating the parasympathetic system. The aim of the study is assess the impact of lateralization on vascular access discomfort and heart rate variability by separately stimulating the right and left vagus nerves with cold application in the neck area.

## 2. Materials and Methods

The study was carried out between 20 February and 30 March 2024 at Samsun University Samsun Training and Research Hospital, following ethics committee approval (GOKAEK 2024/3/9) and Clinical Trials (NCT06253299) registration. Patients arriving in the operating room following anesthesia and surgical prep were informed about the study and their written consent was obtained.

- Study Inclusion Criteria: The study comprised patients between the ages of 18 and 75 who underwent elective surgery and were classified as American Society of Anesthesiologists (ASA) class I-III.
- Study Exclusion Criteria: The study excluded individuals with neurocognitive disorders, patients undergoing oncological treatment, those who had undergone surgery on the back of the hand, individuals with skin disorders, peripheral vascular disease, chronic use of analgesics and steroids, users of gabapentinoids, individuals with substance and alcohol addiction, those with peripheral neuropathy, and pregnant women.
- Randomisation and Intervention: Patients were transferred to and observed in the preoperative waiting room. Sample size for each cohort was calculated to be 70 individuals, accounting for loss to follow-up. Using a lottery system, patients were randomly divided into two groups: Group L (left) and Group R (right). Following standardization of its temperature, a specialized marble stone measuring 4×5 cm was utilized to apply cold to the neck region. Temperature standardization was achieved by placing the stone in the vegetable shelf of a refrigerator set between 4 and 8 °C (degrees Celsius) for 10 minutes (min), leading to a stone temperature of 11 °C that increases to 18 °C after five min of exposure to room temperature. The stone was administered to each patient immediately following its removal from the refrigerator, without any waiting period.
- Group R: Just before the vascular cannulisation, a 4×5 cm cold marble stone was held on the carotid in the right lateral neck region (2–3 cm above the clavicle, on the sternocleidomastoid muscle (SCM)) for 30 seconds, and then cannulisation was performed.
- Group L: Just before the vascular cannulisation, a 4×5 cm cold marble stone was held on the carotid in the left lateral neck region (2–3 cm above the clavicle, on the SCM) for 30 seconds, and then cannulisation was performed.

Heart rate (HR) and noninvasive blood pressure (NIBP) were measured prior to the application of the cold marble to the neck area, 30 seconds after the application as well as before and after the establishment of vascular access. For venous cannulation a skilled practitioner

placed an 18-gauge green coloured catheter on the back of the patient's left hand. The patients were then asked to rate their pain levels on a scale of 0 to 10 using the Numeric Rating Scale (NRS), and this value was recorded. Patients where immediate vascular access was not established were excluded from the study. Another researcher, who was unaware of the lateralization, recorded all data.

### *2.1. Statistical analysis*

Patients' data was analyzed using SPSS 21 and sample size analysis was completed using G*Power 3.1.9.7. Sample size was calculated assuming $\alpha = 0.05$, power $(1-\beta) = 0.80$, and effect size 0.5, with equal distribution amongst the groups. Calculations revealed a sample size of 128, 64 for each group. Considering recording errors and drop outs, 70 people were determined to be included in each group and the total sample size was determined as 140 people. Patients were randomized into 2 groups: Group R (right side) and Group L (left side) using the lottery method. The relationship between the NRS scores of both groups and the HR and NIBB values of the patients before and after marble application as well as after vascular access was examined. Kolmogorov Smirnov and Shapiro Wilk tests were used to assess data for normal distribution. In the analysis of data complying with normal distribution, t-test in independent groups (Independent t-test) and significance test of the difference between two pairs (Paired Samples Test) were used. Mann-Whitney U test was used to analyze data that did not comply with normal distribution. Additionally, Chi-square test was used to compare some data. Mean±Standard deviation (Mean±SD) and percentages were used in descriptive statistics. The results were evaluated with a 95% confidence interval and significance was accepted as $p<0.05$.

## 3. Results

The data of 133 patients (67 in Group L and 66 in Group R) were analyzed (Fig. 1). Both groups were similar in terms of age, gender, and body mass index (BMI) (Table 1).

The initial heart rates and non-invasive blood pressure (NIBP) measurements of the groups were comparable. The average heart rate values following vagal stimulation in both groups were significantly lower than the heart rate values before vagal stimulation. Additionally, the average heart rate values after vascular access were also significantly lower than the values before vagal stimulation ($p<0.001$). In Group R, the mean heart rate following vascular access was determined to be considerably greater than the mean heart rate following vagal stimulation ($p=0.815$) (Table 2).

When comparing the average heart rate values for each time period in Group L and Group R, there was no significant difference observed in the mean heart rate values before vagal stimulation ($p=0.645$), after vagal stimulation ($p=0.971$), and after vascular access ($p=0.656$) between the two groups. Upon examining the heart rate change percentages, it was observed that the heart rate change percentages before and after vagal stimulation in Group L were 5.7±5.8%, while in Group R it was 7.1±7.0%. This indicates that the heart rate variability was greater in Group R. However, it is important to note that this difference was not statistically significant ($p=0.219$). When the NRS values of both groups were examined, the Mean±SD was calculated as 2.64±1.28 in Group L and 2.85±1.62 in Group R, and no difference was observed between the average pain scores of both groups ($p=0.941$).

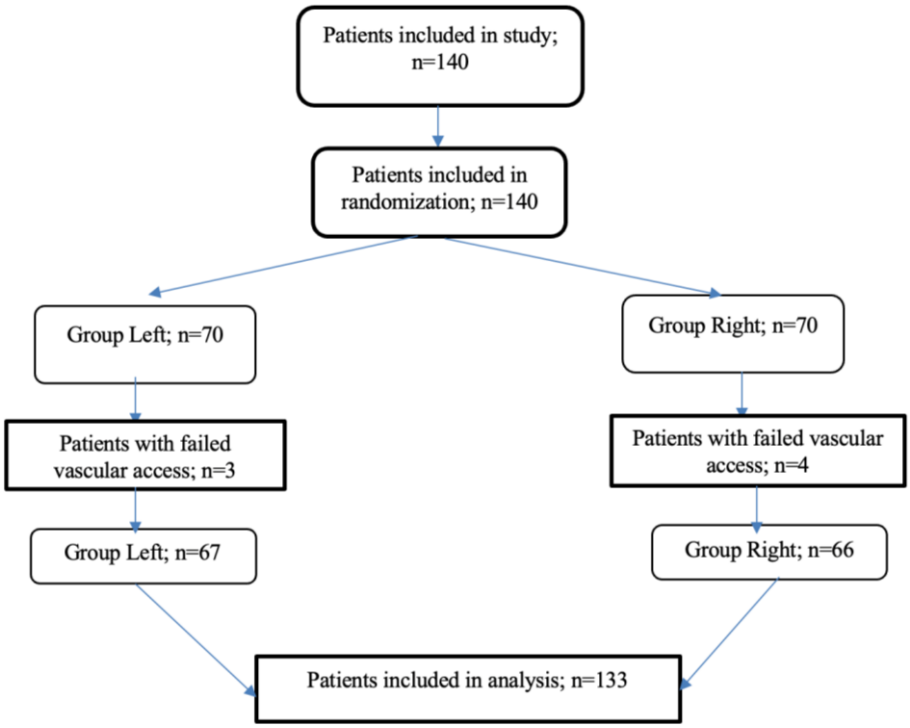


**Fig. 1.** Consort flow chart.

**Table 1.** Demographic data.

| | Group Left (n=67) | Group Right (n=66) | p |
|---|---|---|---|
| Age (years) (Mean±SD) | 52.3±15.4 | 48.0±17.5 | 0.318 |
| Gender (n) M/F | 33/34 | 30/36 | 0.661 |
| ASA (n) I/II/III | 9/53/5 | 11/49/6 | |
| BMI (Mean±SD) | 27.9±5.1 | 28.3±6.6 | 0.935 |

BMI: Body mass index; ASA: American Society of Anesthesiologists; (Mean±SD): Mean±standard deviation; n: Number.

**Table 2.** Heart rate changes.

| Heart rate /minute (Mean±SD) | Group Left (n=67) | p | Group Right (n=66) | p |
|---|---|---|---|---|
| Before vagal stimulation | 77.0±11,8 | <0.001 | 77.9±11.7 | <0.001 |
| After vagal stimulation | 72.5±11.7 | | 72.1±10.1 | |
| Before vagal stimulation | 77.0±11,8 | <0.001 | 77.9±11.7 | <0.001 |
| After vascular access | 72.6±11.8 | | 73.5-10.4 | |
| After vagal stimulation | 72.5±11.7 | 0.815 | 72.1±10.1 | <0.001 |
| After vascular access | 72.6±11.8 | | 73.5-10.4 | |

(Mean±SD): Mean±standard deviation; n: Number.

## 4. Discussion

In an earlier study, we assessed the efficacy of vagus stimulation in alleviating vascular access pain by applying cold bilaterally to the lateral neck region. Our findings demonstrated that vagus stimulation is useful in reducing vascular access pain. Our recent study demonstrates that vagal stimulation does not exhibit any variation in terms of lateralization when used to alleviate vascular access discomfort. In our study, we conducted vagal stimulation by applying cold to the neck region on both the right and left sides, separately. We observed that the average heart rates after vagal stimulation and after vascular access were significantly lower in both groups when compared to the heart rates before vagal stimulation ($p<0.05$). The percentage change in average heart rate after vagal stimulation compared to baseline was greater in Group R than in Group L; however, this difference was not statistically significant ($p>0.05$)

Various techniques are employed for stimulating the vagus nerve, and one of these techniques involves the application of cold to the neck region [12,17]. When individuals experience stress, they instinctively employ techniques that stimulate the vagus nerve, such as splashing cold water on their face and neck, exposing themselves to a breeze, or engaging in deep breathing. Our study preferred the use of cold application as a method for stimulating the vagus nerve and revealed a notable reduction in heart rate in both groups, specifically in the patients who received cold applications to the right and left side of the neck separately. This decrease was observed in comparison to the pre-stimulation period, indicating that stimulation from either side of the neck resulted in vagal stimulation. In their investigation on autonomic modulation in individuals with heart failure, Premchand et al. [18] employed the vagal stimulation approach. One cohort of patients received stimulation from the right hemisphere, while the other cohort received stimulation from the left hemisphere. Upon evaluating the 6-minute walking distance of the patients, it was observed that the group receiving stimulation on the right side had more improvement. The study found that the heart rate, as measured by holter, fell by an average of 3.4 beats per minute in the group stimulated from the left side, and by 4.3 beats per minute in the group stimulated from the right side. Regulation is anticipated to take place through the interplay between the peripheral cardiac nervous system and the central nervous system, irrespective of the side on which the stimulus is applied. In our investigation, we found that applying cold to the right side resulted in a more pronounced decrease in heart rate. However, we did not find a significant difference in variability between left side and right side cold application. Kathrin et al. [19] assessed heart rate variability using vagus stimulation in various auricular localizations. The study's findings indicated that the heart's vagal innervation is asymmetrical.

The sinoatrial node (SAN) receives innervation from the right vagal fibers, while the atrioventricular node (AVN) receives innervation from the left vagal fibers. For instance, when the right neck region is stimulated, it leads to a negative chronotropic impact in the sinoatrial node (SAN), resulting in a decrease in heart rate. Similarly, stimulation of the left neck region creates a negative dromotropic effect in the atrioventricular node (AVN), leading to a slowdown in heart rate. The vagus nerve plays a key role in autonomic regulation of the heart, and its right and left branches exert differential

physiological effects. Right-sided vagus nerve stimulation predominantly affects the sinoatrial node, resulting in a negative chronotropic effect, whereas left-sided stimulation mainly influences the atrioventricular node, leading to a negative dromotropic response [20]. Hendrik et al. [21] investigated the effects of vagus stimulation on pigs. They specifically focused on the neck region and found that there was no significant difference in heart rate variability between stimulation from the right and left sides.

Activation of inhibitory pathways through the nucleus tractus solitarius and subsequent stimulation of other autonomic nuclei centrally leads to the analgesic effect of vagal stimulation [14,22,23]. The activation of the vagus nerve contributes to pain management by reducing inflammation and modulating neuronal activity in pain pathways [2]. In a study conducted by Marcos et al. [3] on rats, it was found that left auricular acupuncture suppressed the transmission of pain signals in the visceral-somatic nociception model. However, this effect was not detected when right auricular acupuncture was employed. The ineffectiveness of lateralization is believed to be attributed to the fact that the analgesic impact of vagal stimulation was a result of central inhibition rather than peripheral nociceptive processes [14]. In their study examining the impact of vagal stimulation on acute and chronic pain, Likar et al. [24] determined that it has the potential to be a remarkable and supplementary alternative to medication for managing chronic and acute postoperative pain.

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*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

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*This study was approved by the ethics committee of Samsun University Samsun Training and Research Hospital, following ethics committee approval (approval number: GOKAEK-2024/3/9; date: 10.01.2024). Written informed consent was obtained from the participants. All methods were performed in accordance with relevant guidelines and regulations.*

***Author Contributions***

*The author confirms sole responsibility for all aspects of the study including: conceptualization, methodology, formal analysis, investigation, data curation, visualization, writing – original draft, and writing – review & editing.*

## 5. Conclusions

In our study, cold application to the right lateral neck region during vagal nerve stimulation produced greater changes in heart rate; however, this difference was not statistically significant. No significant difference was observed between right- and left-sided stimulation in terms of analgesic efficacy. Based on our findings, we suggest that daily cold application to the neck region may contribute to heart rate modulation and provide analgesic benefits. However, our results did not show a clinically significant lateralization effect between the right and left sides. Further studies with larger patient groups are needed to develop a standardized protocol and model for clinical application.

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Challenge Journal of Perioperative Medicine

Research Article

# Radiological evaluation of central venous catheter tip malposition

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## ABSTRACT

**Background:** Malposition of central venous catheters is a potentially severe but often preventable complication. This study aimed to assess the radiological distribution of central venous catheter tip positions and to discuss malposition mechanisms based on anatomical and radiographic literature.

**Methods:** A retrospective analysis of 374 patients who underwent intraoperative central venous catheter insertion between January 2022 and December 2023 was conducted. Radiographs were evaluated using a carina-based classification system: Zones A–C (normal) and Zone D (malposition). Data were analyzed retrospectively.

**Results:** The right internal jugular vein was the most commonly preferred access site, used in 80.0% of cases. Zone A: 52.3%, Zone B: 18.5%, Zone C: 17.8%, Zone D (malposition): 11.4%. There was no statistically significant association between catheter size and malposition ($p>0.05$).

**Conclusion:** Utilizing the carina as a reference point during post-procedural imaging is essential for accurate catheter tip localization. Adjunctive modalities—including intracavitary ECG, ultrasound, and radiography—contribute to complication reduction and procedural safety.

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## 1. Introduction

Central venous catheters (CVC) are fundamental to modern intensive and perioperative care. Despite the widespread use of ultrasound guidance, catheter malposition remains a frequent and clinically relevant complication, with reported rates between 5% and 15%. Accurate tip positioning is essential to prevent serious outcomes such as vascular erosion, thrombosis, retrograde cerebral infusion, or cardiac tamponade [1,2].

Malposition often reflects anatomical variability or physiological factors—such as thoracic vein angulation, patient positioning, or respiratory motion—rather than procedural error. Left-sided insertions, particularly via the internal jugular (IJV) or subclavian veins (SV), carry a higher risk due to the longer, angled course of the left brachiocephalic vein. Additionally, tip migration may occur post-procedure due to body movement or intrathoracic pressure changes [1,3].

Raptis et al. [3] proposed a radiographic classification based on tip position relative to the midline, which aids in identifying malposition. Although ultrasound is integral to placement, chest radiography remains the standard for verifying position and detecting complications. This study evaluates catheter tip positions using the carina as a radiological landmark and explores contributing factors to malposition through anatomical and clinical analysis.

## 2. Materials and Methods

This retrospective single-center observational study was conducted from January 2022 to December 2023 at

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a tertiary academic hospital. Postoperative chest radiographs and patients' archival data were reviewed, and tip positions, as illustrated in Fig. 1, were classified as follows:

- Zone A: Optimal position (1–2 cm above/below carina),
- Zone B: Superior deviation from the carina,
- Zone C: Caudal deviation,
- Zone D: Malposition (e.g., carotid artery, azygos vein, thoracic duct).

It was determined that Thoracic CT was evaluated in 15 of 325 patients, based on abnormal chest X-ray or clinical suspicion of malposition.

Patients without post-procedural chest imaging, inaccessible data, or femoral catheter placement were excluded. Demographic data, insertion site, catheter type, and radiological findings were recorded. SPSS 23.0 was used. Chi-squares test was applied ($p<0.05$ significant).

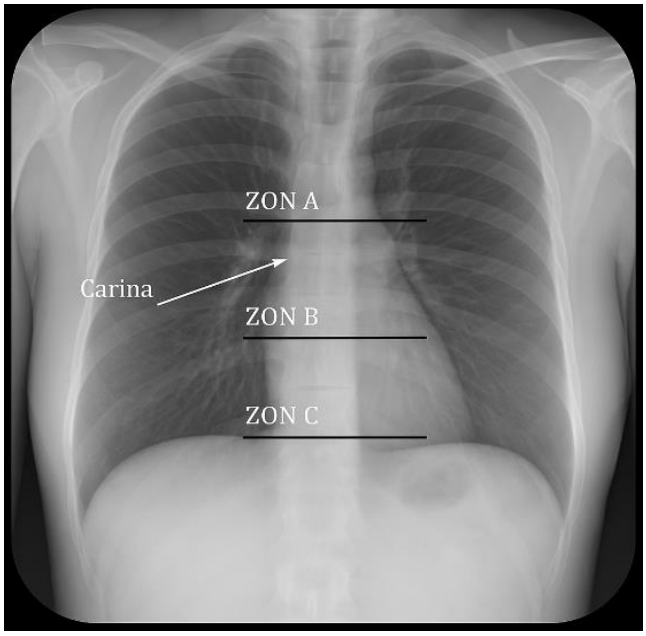


**Fig. 1.** Zone classification of CVC tip positions on chest radiograph.

## 3. Results

A total of 374 patients were initially considered for inclusion in the study. However, 49 patients (13.1%) were excluded due to missing or non-diagnostic imaging, inaccessible data, or femoral catheter placement, resulting in a final cohort of 325 patients. The mean age of 59.4 ± 16.5 years; 40.61% (n=132) of the cohort were female and 59.38% (n=193) were male. Among the 325 central venous catheters analysed, the majority were inserted via the right internal jugular vein (269 cases, 80.0%), followed by the right subclavian vein (45 cases, 13.8%), the left internal jugular vein (13 cases, 4.0%), the left subclavian vein (7 cases, 2.2%). There was no statistically significant difference in malposition rates between thoracic vascular access routes, such as jugular and subclavian catheterizations (p=0.342).

Radiological evaluation of catheter tip location, as illustrated in Fig. 2(a–b), revealed the following distribution across predefined zones: Zone A in 52.3% (n=170), Zone B in 18.5% (n=60), Zone C in 17.8% (n=58), and Zone D in 11.4% (n=37). The overall malposition rate was 11.3%, consistent with the 5–15% range reported in prior studies.

All central venous catheterizations were performed using the Seldinger technique. In 34% of the cases, catheter insertion was guided by real-time ultrasound, whereas in 66%, anatomical landmark guidance was utilized. All procedures were conducted by an anesthesiology specialist or residents with a minimum of 1 year of supervised clinical training. The intracavitary electrocardiographic (ECG) confirmation technique was not employed for tip verification. Additionally, statistical comparison revealed no significant difference in the rate of catheter malposition between ultrasound-guided and landmark-guided insertion (p=0.217).

Among the catheters classified as Zone D, 29 extended caudally into the inferior vena cava (IVC); 3 were malpositions into the carotid artery, and 5 had traversed into the contralateral IJV. These findings emphasize the role of over-insertion and right-sided access in catheter malposition.

No significant difference in malposition rates was observed among the catheter types—7F 20 cm: 10.0% (13/130), 7F 16 cm: 9.4% (9/96), and 8F 20 cm: 17.1% (12/70)—with $\chi^2$=2.91 and p=0.234. Collectively, these three catheter types accounted for 91.9% (34/37) of all malposition cases. Similarly, there was no statistically significant association between malposition and either patient sex, catheter entry site, body length, patient height, or body mass index.

## 4. Discussion

The malposition rate observed in this study is consistent with the literature, which reports rates ranging from 5% to 15%, depending on access site, insertion technique, and imaging confirmation protocols. The most frequent malposition pattern was caudal advancement of the catheter into the IVC. This was likely caused by excessive insertion length or undetected resistance during guidewire advancement, particularly in right-sided access. Similar findings have been reported by Yilmazlar et al. [4], emphasizing that right atrial or IVC positioning remains a persistent issue despite ultrasound guidance.

Although less common, arterial malposition—such as inadvertent cannulation of the carotid artery—remains a high-risk complication that requires immediate recognition and prompt management. If arterial puncture is suspected, especially during right IJV access, pressure transduction, pulsatile blood flow, or bright red blood return should raise concern. In cases where a large-bore catheter has already been inserted into the carotid artery, blind removal is contraindicated due to the risk of catastrophic hemorrhage, stroke, or pseudoaneurysm formation. Current guidelines and expert consensus rec-

ommend urgent consultation with vascular or cardiothoracic surgery when such an event occurs. Surgical intervention is generally preferred for definitive repair, especially in hemodynamically stable patients, and should ideally take place in a controlled operative setting. Endovascular repair—such as covered stent placement—may be considered in selected cases or high-risk surgical candidates, particularly when performed in hybrid operating suites with imaging guidance. Ultrasound-guided insertion and real-time verification methods (e.g., dynamic needle tip positioning, compressibility tests) significantly reduce the likelihood of arterial injury. Still, awareness and readiness for immediate surgical involvement remain essential in managing this life-threatening complication [4–7].

In the present study, cases of carotid artery cannulation were promptly evaluated and managed by cardiovascular surgery teams, and catheter removal was performed under surgical supervision to minimize the risk of complications.

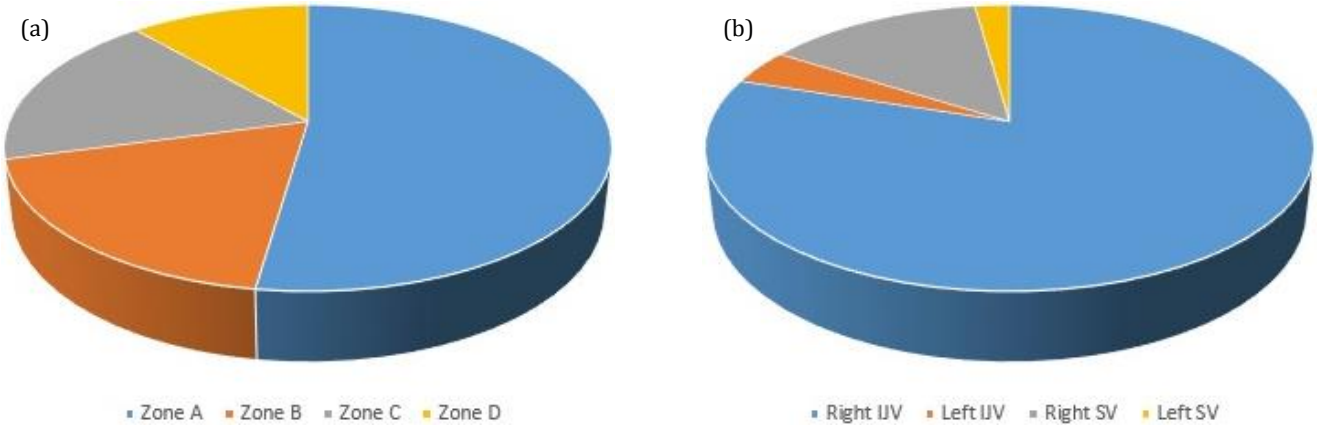


**Fig. 2.** (a) Zone-based evaluation of CVC tip positions in jugular and subclavian insertions (Zone A 52.3%, Zone B 18.5%, Zone C 17.8%, Zone D 11.4%);
(b)Vascular access site distribution of all thoracic central venous catheters (Right IJV 80% (269), Left IJV 4.0% (13), Right SV 13.8% (45), Left SV 2.2% (7)).

Previous research has shown that catheter malpositions may appear deceptively appropriate on anterior-posterior chest radiographs, especially in cases where the catheter loops or deviates into mediastinal tributaries. This underscores the potential limitations of standard radiography and supports the use of additional imaging techniques when clinically indicated [8]. Although chest radiography remains the first-line tool for verifying tip location, its two-dimensional limitations can obscure atypical courses, especially in anatomically complex cases. In such scenarios, adjunctive imaging modalities—such as contrast-enhanced studies, computed tomography, or bedside ultrasound—play a crucial role in ensuring accurate assessment. The carina has emerged as a consistently reliable radiological landmark for tip evaluation, offering improved localization accuracy over vertebral body references. Furthermore, multimodal approaches have been advocated, particularly in the presence of anatomical variants or suspected malposition into atypical sites such as the azygos vein, internal mammary vein, or the pericardiophrenic recess [8,9]. Supporting this, Nifong and McDevitt [10] demonstrated that incorporating computed tomography verification can significantly reduce false-negative interpretations associated with standard radiographs in complex clinical situations.

Preventive strategies should include standardized use of real-time ultrasound guidance, enhanced operator training, and deliberate attention to anatomical landmarks during insertion. Recent studies have also demonstrated the effectiveness of intracavitary electrocardiography (IC-ECG) using P-wave amplitude monitoring to identify the cavoatrial junction in real time. As the catheter tip approaches the SVC–RA junction, a rising P-wave amplitude followed by biphasic or negative morphology indicates, respectively, optimal positioning or over-insertion. According to Schummer et al. [11], IC-ECG offers superior tip localization and reduces malposition risk compared to traditional landmark-based techniques.

Furthermore, no statistically significant correlation was identified between catheter size and malposition; however, a subtle trend toward higher malposition frequency was observed in larger size catheters. This may be due to increased stiffness or excessive advancement. Gibson and Bodenham [1] have suggested that catheter diameter and rigidity may influence directional control, especially in angled venous segments. Similarly, while malposition was slightly more common among male patients, this did not reach statistical significance. Differences in thoracic anatomy and vascular angles between the sexes may affect catheter direction and warrant further investigation.

Overall, the findings underscore the need for multimodal verification techniques and tailored insertion strategies to minimize the risk of malposition and enhance procedural safety. Peres has highlighted that combining methods such as IC-ECG and radiographic imaging provides a higher degree of confidence in confirming correct tip location [1,12]. Furthermore, as emphasized by Kornbau et al. [6], malpositioned catheters should not be considered minor technical deviations, as they carry increased risk of thrombosis, cardiac tamponade, and therapeutic failure.

### *4.1. Limitations*

This study has several limitations. Its retrospective, single-center design may limit the generalizability of the findings. In preoperative procedures, data regarding the use of ultrasound guidance, reliance on anatomical landmarks, or the occurrence of possible carotid artery puncture without catheter insertion were not available. Furthermore, the relationship between patient thoracic diameter and the length of the catheter selected could not be systematically assessed.

## 5. Conclusions

This study underscores the ongoing relevance of carina-referenced imaging in identifying CVC malposition. The observed malposition rate highlights that technical proficiency alone is insufficient without reliable post-placement verification. Notably, the most common malposition pattern observed involved caudal migration of the catheter into the IVC, highlighting the need for increased vigilance, particularly in right-sided insertions. The findings support the routine use of carina-based chest radiography, ideally complemented by adjunctive modalities such as intracavitary ECG and ultrasound, to improve tip localization and minimize the risk of complications. Beyond clinical practice, the integration of these verification strategies into procedural training programs may contribute to reducing malposition rates. Accurate catheter tip positioning is not merely a procedural detail, but a determinant of patient safety, infection risk, and long-term vascular outcomes. Standardizing these verification protocols across surgical and intensive care settings is essential for enhancing procedural safety and improving overall patient care.

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***Author Contributions***
***Meltem Ceylan Delice:*** *conceptualization, data curation, investigation, formal analysis, writing – original draft, visualization.*
***Nilgun Kavrut Ozturk:*** *methodology, validation, supervision, writing – review & editing, project administration.*

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Challenge Journal of Perioperative Medicine

Case Report

# Awake laparoscopic cholecystectomy under thoracal segmental spinal anesthesia and intermediate cervical plexus block: A case series

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**ABSTRACT**

Laparoscopic cholecystectomy (LC) is the preferred approach for treating gallstone disease because of its minimally invasive characteristics. However, factors such as increased intra-abdominal pressure, pneumoperitoneum, and positional changes present significant challenges in anesthetic management. While LC is typically performed under general anesthesia, thoracic segmental spinal anesthesia and cervical plexus block have emerged as effective alternatives in patients for whom general anesthesia poses a high risk. This study reports the use of thoracic spinal anesthesia combined with cervical plexus block in patients where general anesthesia is considered risky. After obtaining informed consent for awake laparoscopic surgery, anesthesia was managed under appropriate monitoring. The combination of spinal anesthesia and cervical plexus block allowed for the successful completion of the procedure, with minimal complications observed in the early postoperative period. In conclusion, thoracic segmental spinal anesthesia and intermediate cervical plexus block offer a safe and effective alternative for patients at high risk for general anesthesia.

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## 1. Introduction

Laparoscopic cholecystectomy (LC) is viewed as a less invasive option compared to open surgery, offering benefits like smaller incisions, less postoperative discomfort, and quicker recovery times. It is commonly recognized as the preferred method for treating gallstone disease. However, despite its benefits, the procedure presents significant challenges in anesthetic management, particularly due to hemodynamic changes caused by increased intra-abdominal pressure, pneumoperitoneum, and positional changes [1].

Although LC is typically performed under general anesthesia, studies and case reports also describe its performance as awake under regional anesthesia [1–3]. Shoulder pain, which occurs in awake patients and can compromise patient comfort, as well as increase the need for additional anesthetic and analgesic intervention, also arises postoperatively in patients undergoing general anesthesia. To mitigate shoulder pain in laparoscopic surgeries, various regional techniques and pharmacological agents have been employed [4,5].

This case series aims to report the use of thoracic spinal anesthesia combined with cervical plexus block in patients at our clinic for whom general anesthesia posed significant risks.

## 2. Case Presentation

The descriptive characteristics of the patients are presented in Table 1.

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**Table 1.** Descriptive characteristics of patients.

| Age | Gender | Risk for general anesthesia | Duration of Surgery (min) | Total dose of ephedrine (mg) | Total dose of analgesic (gr paracetamol) |
|---|---|---|---|---|---|
| 68 | Male | COPD | 50 | 20 | 1 |
| 45 | Female | Interstitial pulmoner fibrosis | 30 | 10 | 0 |
| 38 | Male | Difficult airway | 80 | 10 | 2 |
| 43 | Female | Difficult airway | 65 | 0 | 0 |
| 20 | Male | Myotonic Dystrophy | 30 | 10 | 1 |
| 59 | Female | History of failed intubation | 50 | 0 | 2 |
| 26 | Male | History of anaphlyaxis to intravenous anesthetic agents | 35 | 10 | 3 |
| 63 | Male | COPD | 40 | 20 | 1 |

COPD: Chronic obstructive pulmonary disease.

The patients, whose descriptive characteristics are specified, were informed about the risks of general anesthesia and the plan for awake surgery under regional anesthesia. Informed written consent was obtained from all patients.

After being brought into the operating room, the patients were monitored with non-invasive arterial blood pressure, electrocardiography, and pulse oximetry. A 20G IV catheter was placed in the cubital region, and crystalloid infusion was initiated. After positioning the patients in the supine position with their heads turned to the opposite side, the midpoint of the sternocleidomastoid (SCM) muscle was identified, and the ultrasound probe was applied to visualize both the SCM muscle, investing fascia and the prevertebral fascia. An echoic 50mm peripheral nerve block needle (UltraplexTM, B.Braun, Melsungen AG, Germany) was used to inject 5-10 mL of 0.25% bupivacaine (Buvicaine 0.5%, 5 mg/ml Polifarma) into the intermediate cervical plexus (Fig. 1).

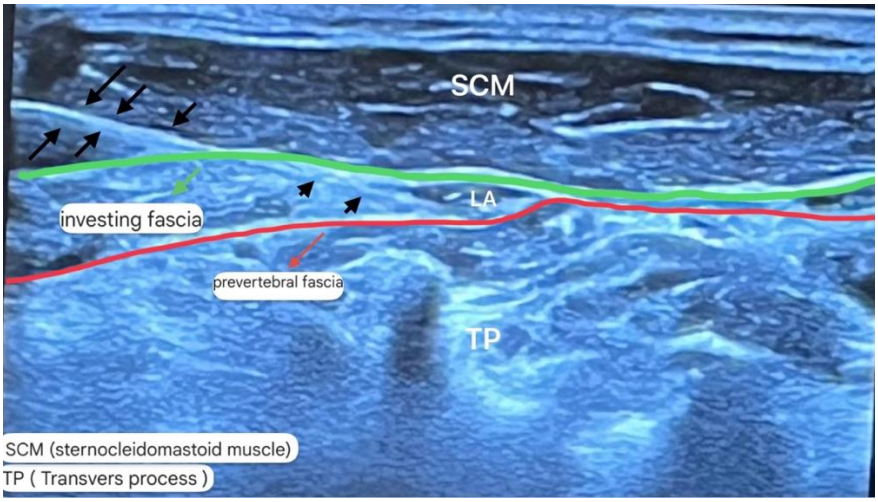


**Fig. 1.** Ultrasound image of the intermediate cervical plexus block.

Once the patients were seated and sterile conditions were ensured, a paramedian approach was used to access the subarachnoid space through the T7-8 intervertebral space with a 26G pencil-point spinal needle. After observing the flow of cerebrospinal fluid, 7.5 mg of bupivacaine (Buvicaine 0.5%, 5 mg/ml Polifarma) and 25 mcg of fentanyl (Talinat 0.5 mg/10 mL, Vem İlaç, Çerkezköy, Türkiye) were administered to induce spinal anesthesia. Sensory block was assessed after the procedure using the pinprick test, and sensory block between T4-L1 was confirmed before starting the surgery. Oxygen support was provided, and capnography was used for respiratory monitoring. 0.02 mg/kg midazolam was administered to patients that experiencing anxiety or discomfort. Due to the risk of conversion to general anesthesia caused by failed spinal block, prolonged surgical duration, and surgical complications, difficult airway equipment (e.g., laryngeal mask airway, video laryngoscope) was prepared in the operating room for patients preoperatively assessed as having a difficult airway. For the patient with a history of anaphylaxis, equipment for rapid fluid resuscitation and airway management was prepared. Adrenaline for intravenous use was readily available in the operating room. In case of hypotension (20% or greater decrease in mean arterial pressure compared to the baseline measurement), ephedrine and atropine were planned for bradycardia (heart rate < 50bpm) (Fig. 2).

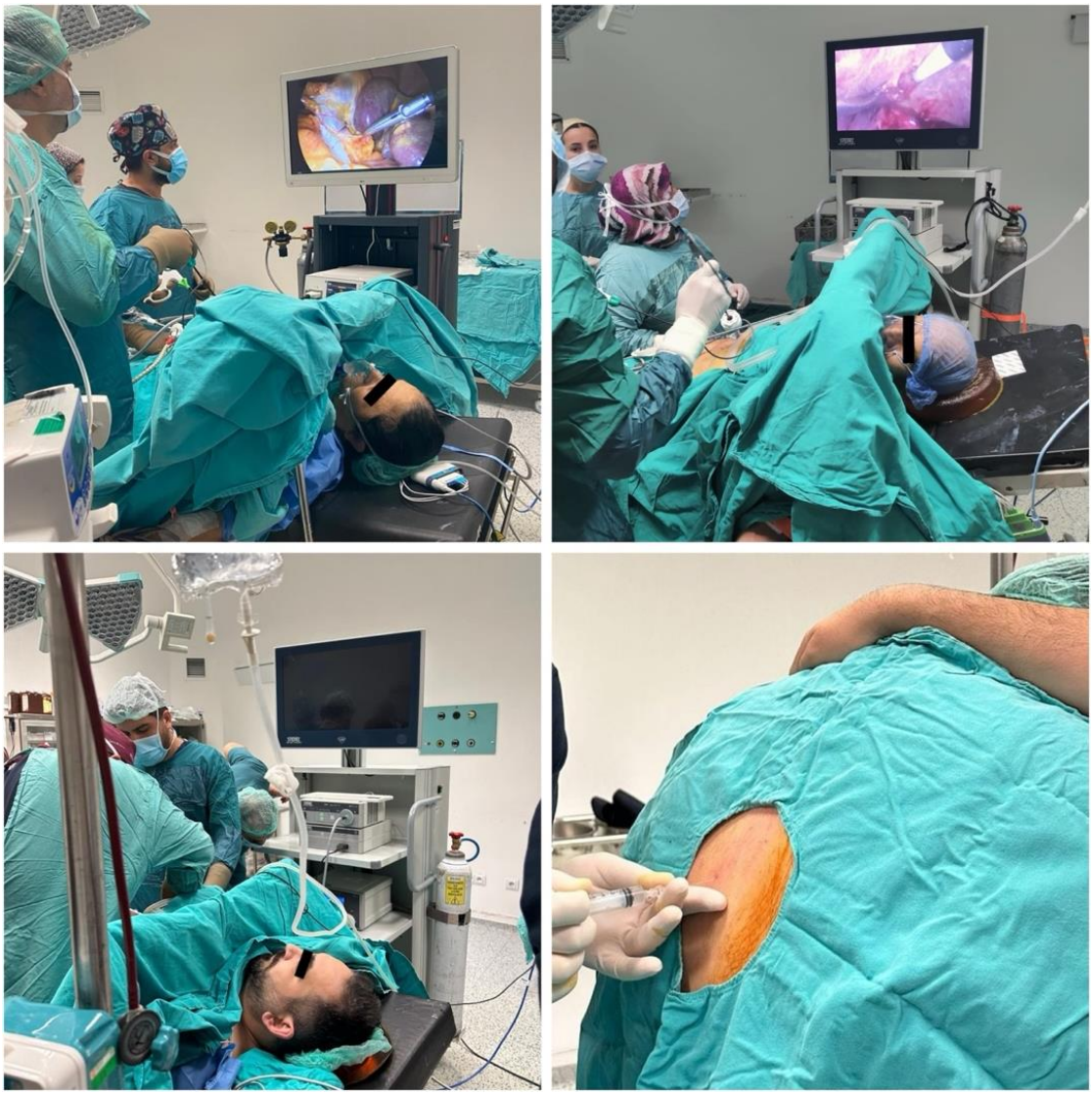

**Fig. 2.** Intraoperative status of the patients.

The surgery was performed using the standard 3 or 4 port technique. During both the insufflation phase and the surgical procedure, the intraperitoneal pressure was maintained at 8-10mmHg. The anesthesia management was found to be effective and successful in all patients. Mild hypotension was observed early in the postoperative period in all patients, which was controlled with ephedrine (10 mg-20mg). No bradycardia, respiratory depression, or apnea was observed.

Mild shoulder pain was noted in two patients, but no additional analgesic or anesthetic agents were administered. At the end of the surgery, patients were monitored in the recovery room for at least 30 minutes before being transferred to the surgical ward. During the postoperative period, neurological and pain assessments were conducted on the patients. For pain assessment, the Numeric Rating Scale (NRS) was used. Patients with a pain score of 4 or higher during the first 24 hours were administered 1 gram of paracetamol. No complications (such as hypotension, bradycardia, respiratory depression, apnea, back pain, paresthesia, or radiculopathy) were encountered during the first 24 hours of monitoring.

## 3. Discussion

Thoracic spinal anesthesia has become a viable and effective option for patients at high risk for general anesthesia. It has been safely and successfully utilized in various procedures, such as breast surgeries, abdominal cancer surgeries, nephrectomy, and laparoscopic operations [6]. van Zundert et al. [2] have reported that thoracic segmental spinal anesthesia can be safely and effectively applied in laparoscopic cholecystectomy surgeries. Ellakany [1], in a study comparing general anesthesia and thoracic segmental spinal anesthesia in laparoscopic cholecystectomy, found that the spinal anesthesia group had a shorter discharge time and higher satisfaction rates.

Shoulder pain in laparoscopic surgeries is often attributed to irritation of the phrenic nerve branches arising from the C3-C5 roots. Because cervical plexus blocks can target the cervical roots, they have been used to prevent shoulder pain during laparoscopic surgeries. Kanawati et al. [7], in a case series of awake sleeve gastrectomy, reported that a combination of spinal anesthesia and superficial cervical plexus block was sufficient in

preventing both surgical and shoulder pain. Another study showed that cervical plexus block under spinal anesthesia was effective in preventing shoulder pain during laparoscopic surgeries, with ultrasound-guided blocks proving to be superior to the landmark method [8]. Intravenous dexmedetomidine, used for sedative and analgesic purposes, was compared with cervical plexus block for preventing shoulder pain in laparoscopic surgeries, and it was found that the cervical plexus block was more effective [9]. Although the superficial cervical plexus block is considered easier and safer among cervical plexus blocks, the intermediate cervical plexus block has been shown to provide deeper and more potent analgesia in deep tissues contributing to the visceral distribution of pain [10]. In robotic-assisted laparoscopic prostatectomy, intermediate cervical plexus block, performed alongside thoracic spinal anesthesia, enabled the surgery to be conducted in an awake state [11].

## 4. Conclusions

In conclusion, we believe that thoracic segmental spinal anesthesia combined with intermediate cervical plexus block provides an effective and efficient anesthetic management option for awake surgery in patients for whom general anesthesia is risky.

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***Author Contributions***
***Nezir Yilmaz:*** *conceptualization, investigation, methodology, patient management, writing – original draft, visualization, supervision.*
***Yunus Bozok:*** *validation, data curation, writing – review & editing.*

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Challenge Journal of Perioperative Medicine

Case Report

# Tonsillectomy in a pediatric patient with propionic acidemia: Anesthesia management and potential perioperative challenges

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## ABSTRACT

Propionic acidemia (PA) is a rare metabolic disorder caused by a deficiency in the propionyl-CoA carboxylase enzyme, leading to the accumulation of toxic metabolites. Surgical procedures pose a risk of metabolic decompensation in patients with PA, requiring careful anesthesia management. A four-year-old male patient with propionic acidemia was scheduled for tonsillectomy due to recurrent upper respiratory tract infections. Midazolam was administered for premedication, and anesthesia induction was achieved with thiopental and rocuronium. Anesthesia maintenance was provided with sevoflurane, and fentanyl was used for analgesia. Postoperative pain management included paracetamol. The procedure was completed without complications, and the patient was transferred to the ward in stable condition. Anesthesia management in PA patients should focus on maintaining metabolic stability. This case demonstrates that with proper preoperative preparation, careful anesthesia management, and close perioperative monitoring, surgical interventions can be safely performed in pediatric patients with PA.

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## 1. Introduction

Propionic acidemia (PA) is a rare autosomal recessive metabolic disease caused by deficiency or dysfunction of the enzyme propionyl-CoA carboxylase [1]. It occurs as a result of pathogenic mutations in the PCCA or PCCB genes. These genes encode the enzyme propionyl-CoA carboxylase, which is found in mitochondria. Propionyl-CoA carboxylase is involved in the catabolism of branched-chain amino acids, the process by which proteins are broken down for cellular metabolism. Enzyme deficiency results in the accumulation of propionic acid and related metabolites (propionyl-CoA, 2-methylcitrate, 3-OH-propionate). Accumulation of these toxic metabolites may lead to secondary mitochondrial dysfunction, resulting in progressive organ damage [2]. This prevents the conversion of propionyl-CoA to methylmalonyl-CoA and leads to the accumulation of toxic metabolites, resulting in clinical symptoms such as metabolic acidosis, ketosis and hyperammonemia [1]. Surgical procedures in patients with PA require careful management of anesthesia, as they can cause serious complications due to increased metabolic stress [3].

Significant metabolic abnormalities, including low levels of free carnitine, elevated C3 propionyl carnitine, and varied amino acid imbalances may be present [4]. Main challenges related to this rare case are higher incidence of cardiac manifestations like dilated cardiomyopathy due to accumulation of toxic metabolites and in-

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flammation in the heart muscle, long QT syndrome, life threatening arrythmias [5] white matter involvement and ventricular dilatation, acute decompensation caused by the catabolic stress of surgery and liver disease as propionyl-CoA carboxylase is primarily expressed in the liver [6].

Tonsillectomy is a common surgical procedure performed in children, but anesthetic management in patients with metabolic diseases such as PA poses challenges. This case report discusses the anesthetic management during tonsillectomy of a 4-year-old boy with PA and the challenges encountered in the perioperative period.

## 2. Case Presentation

A four-year-three-month-old, 13-kg male child diagnosed with propionic acidemia was scheduled for tonsillectomy due to frequently recurring upper respiratory tract infections and was taken into surgery. The patient's PA diagnosis was made on the third day of life and he was regularly followed up by a pediatric metabolic diseases specialist. The patient is on a special protein-restricted diet and is taking carnitine, carglutamic acid and vitamin B12 supplements. The patient, who had no history of seizures and was metabolically stable, was prepared for surgery.

During the premedication phase, 1.3 mg midazolam was administered intravenously to the patient and he was taken to the operation room. The patient's vital signs were monitored and his pulse was measured as 123/min, SpO2 was 94% and blood pressure was 98/54 mmHg. Fingertip blood sugar was measured as 137 mg/dL. 65 mg thiopental was administered for anesthesia induction and neuromuscular blockade was achieved with 9 mg rocuronium. For analgesia, 15 mcg fentanyl was used and the patient was intubated with a size 4.5 cuffed endotracheal tube.

Anesthesia was maintained with sevoflurane MAC (minimum alveolar concentration) 1.3 during the operation and the surgery lasted 35 minutes. Estimated blood loss was 40 ml and the total amount of crystalloid administered intravenously to the patient was 200 ml 5% dextrose-0.45% NaCl. Venous blood gases were obtained at the end of the case (Table 1). 10 meq sodium bicarbonate was administered as a slow infusion in the fluid. 130 mg paracetamol was administered intravenously and 50 mg sugammadex was given to reverse the neuromuscular blockade.

The patient was extubated and taken to the PACU for close monitoring. Inhaled adrenaline and cold steam were administered. In our clinic, inhaled adrenaline and cold steam are routinely administered to pediatric patients undergoing head and neck surgery. In our case, their use was specifically indicated due to the patient's tonsillectomy procedure. He was transferred to the ward with stable vital signs. Early pediatric consultation was performed for nutrition. No respiratory distress was observed in postoperative follow-ups. Postoperative analgesia was provided with paracetamol.

**Table 1.** Intraoperative venous blood gas results.

| | |
|---|---|
| pH | 7.24 |
| $pCO_2$ | 28.2 mmHg |
| $pO_2$ | 99 mmHg |
| $sO_2$ | 96.5% |
| Glucose | 169 mg/dL |
| Lactate | 1.7 mmol/L |
| SBE | -14 |
| $HCO_3$ | 11.9 mmol/L |

pCO2: Partial Pressure of Carbon Dioxide; pO2: Partial Pressure of Oxygen; sO2: Oxygen Saturation; SBE: Standard Base Excess; HCO3: Bicarbonate.

## 3. Discussion

The general anaesthetic management without any complications for tonsillectomy of an infant with PA has been described in this case report, with thoroughly monitoring vital signs along with blood gas analysis to track the metabolic state. Anesthesia management in patients diagnosed with propionic acidemia (PA) carries certain risks due to the nature of the disease. The main goal in anesthesia management in these patients is to prevent metabolic decompensation and minimize potential complications of surgical stress [7]. The most important problems that patients with PA may encounter during surgical procedures include metabolic acidosis, hypoglycemia, hyperammonemia and electrolyte imbalances [8]. Therefore, anesthesia management is critical.

In preoperative preparation, the patient's metabolic status should be stabilized prior to surgery. This includes careful monitoring of blood glucose levels, electrolytes, and acid-base balance. In patients on a protein-restricted diet, appropriate dietary adjustments should be made to ensure adequate energy intake in the preoperative period [9]. Fast and short-acting anesthetic agents should be preferred during the induction phase [7]. Propofol should not be preferred as an induction agent because it contains polyunsaturated fatty acids [10]. These agents can reduce metabolic load and provide rapid recovery. Agents such as thiopental and sevoflurane can be used safely in patients with PA; however, the metabolic effects of these agents should be closely monitored. In our case, we used thiopental for induction and sevoflurane for maintenance.

Opioid doses should be carefully adjusted in analgesia management. Short-acting opioids, especially fentanyl, should be preferred [7]. Due to the short duration of the case, no opioids were administered except for 15 mcg fentanyl before ETE (endotracheal intubation). Close perioperative monitoring is important. Blood glucose levels, electrolytes and acid-base balance should be checked frequently during surgery. Constant monitoring is required due to risk of hypoglycemia.

Fluid management of patients should be planned carefully. Hypotension and hypovolemia may lead to increased metabolic stress [11]. In postoperative follow-up, patients should be closely monitored and a nutritional regime should be provided in the early period.

Non-opioid analgesics should be preferred in postoperative pain management [12]. Agents such as paracetamol are safe because their metabolic side effects are minimal.

Given the patient's underlying diagnosis of propionic acidemia, the use of propionic acid derivatives, including ibuprofen, naproxen, and ketoprofen, is generally discouraged due to the potential risk of exacerbating metabolic derangements. These medications can contribute to the accumulation of propionic acid and its toxic metabolites, potentially leading to metabolic decompensation [13]. Therefore, to minimize any metabolic risks, we opted for paracetamol as the primary analgesic agent in this case. Continuous monitoring for signs of metabolic decompensation should be performed and, if necessary, action should be taken in collaboration with a metabolic disease specialist [14].

## 4. Conclusions

Anesthesia management in patients with PA requires a multidisciplinary approach. The risk of complications can be minimized with close cooperation between the anesthesia team, surgeon, and metabolic specialists. Safely performing the surgical procedure while maintaining metabolic balance forms the basis of successful anesthesia management in this patient group. This case report emphasizes the importance of careful anesthesia application in patients with PA and demonstrates that surgical procedures can be managed successfully.

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***Conflict of Interest***

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***Data Availability***

*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

***Ethics Approval and Consent to Participate***

*Written informed consent was obtained from the parents of all infants that were found to be eligible to be included in the study, prior to study enrollment.*

***Author Contributions***

***Mehmet Akif Yilmaz:*** *literature review, visualization, investigation, writing – original draft.*
***Gokhan Tekin:*** *formal analysis, investigation, writing – review & editing.*
***Berivan Bozan:*** *investigation, validation, writing – review & editing.*
***Mirac Selcen Ozkal Yalin:*** *data curation, patient care, writing – review & editing.*
***Nuray Uzun:*** *investigation, perioperative monitoring, data curation.*
***Muhammed Enes Aydin:*** *conceptualization, methodology, writing – review & editing, supervision, project administration.*

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Challenge Journal of Perioperative Medicine

Case Report

# Ultrasound-guided supraclavicular nerve and interscalene block for clavicle surgery in pregnancy: A case report and case-based literature review

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**ABSTRACT**

A 34-year-old woman at 32 weeks of gestation sustained a displaced clavicle fracture following a motor vehicle accident. To avoid the risks of general anesthesia during late pregnancy, ultrasound-guided interscalene and selective supraclavicular nerve blocks were performed with a single skin entry point. Surgery was completed uneventfully, and there was no need for additional analgesics. No maternal or fetal complications observed. This case illustrates the safety and efficacy of regional anesthesia in pregnant trauma patients and highlights the potential of targeted peripheral nerve blocks as a viable alternative to general anesthesia for upper extremity surgeries during pregnancy.

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## 1. Introduction

Trauma is one of the leading non-obstetric causes of maternal mortality, and the third trimester presents increased risks for both mother and fetus [1]. Although orthopedic trauma requiring surgical intervention is rare during pregnancy, clavicle fractures present a unique anesthetic challenge due to their complex innervation and the high risk associated with general anesthesia in pregnant patients.

Regional anesthesia has emerged as a safer alternative for clavicle surgery in such patients. Selective supraclavicular nerve blocks, when combined with interscalene blocks, allow for targeted analgesia while minimizing local anesthetic volume and systemic exposure [2]. An interscalene block is a regional anesthetic technique that targets the roots of the brachial plexus, typically used for shoulder and upper arm surgeries [3]. The supraclavicular nerve block, on the other hand, targets the superficial sensory branches that supply the skin overlying the clavicle and upper chest [4]. However, their use in pregnant trauma patients remains sparsely documented.

Here, we describe the successful use of a single-entry-point, ultrasound-guided interscalene and selective supraclavicular nerve block technique in a woman at 32 weeks' gestation undergoing clavicle fracture repair.

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This case was conducted with written informed patient consent for the publication of this case report and in accordance with institutional ethical guidelines.

## 2. Case Presentation

A 34-year-old woman at 32 weeks of gestation presented to the emergency department following a motor vehicle collision. Evaluation revealed a left distal clavicle fracture, for which surgical repair was planned by the orthopedics department (Fig. 1).

Obstetric consultation confirmed stable vital signs, a soft abdomen without guarding or rebound tenderness, and positive fetal heart tones with a reactive non-stress test. Ultrasonography showed a normal amniotic fluid index, normal placental location with no signs of abruption, and normal umbilical artery Doppler flow. No uterine contractions were observed. It was concluded that there were no obstetric contraindications for surgery. To minimize fetal exposure during surgery, the use of a lead apron was recommended. The patient had no known systemic illnesses, laboratory values were within normal limits, and her ASA physical status was evaluated as class II.

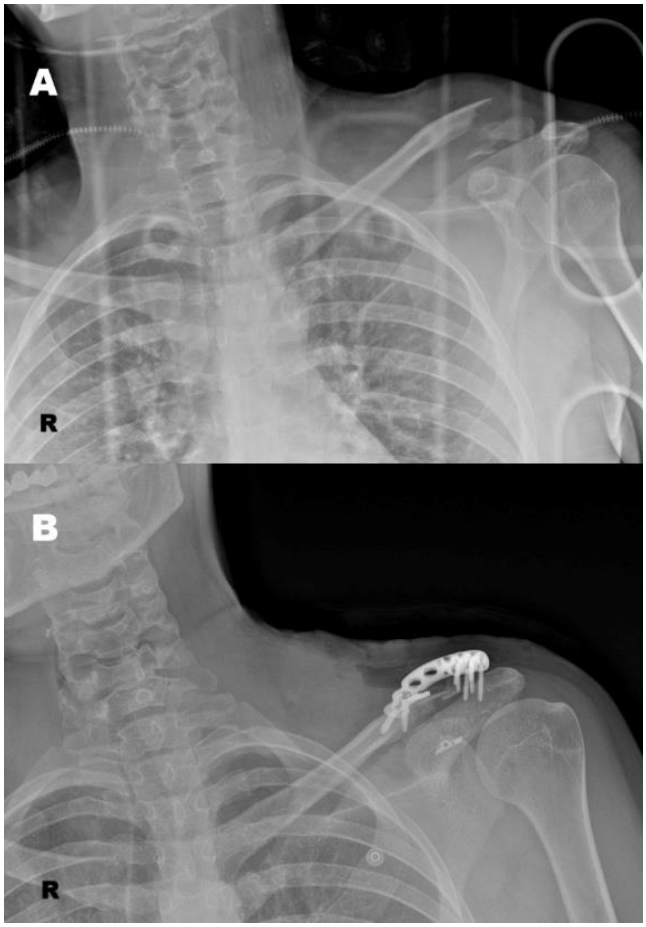


**Fig. 1.** (a) Preoperative anteroposterior chest X-ray demonstrating a displaced fracture of the left distal clavicle; (b) Postoperative radiograph showing internal fixation of the clavicle fracture using a precontoured locking plate.

Upon admission to the operating room, light sedation was achieved with 1 mg of intravenous midazolam. Preoperative vital signs were as follows: $SpO_2$ 97%, blood pressure 137/88 mmHg, and heart rate 87 bpm. We decided to perform a single-entry interscalene and selective supraclavicular nerve block for our patient.

The interscalene block was performed first. With the patient in the supine position and the head turned to the contralateral side, the skin was prepared under sterile conditions. A 5–12 MHz linear ultrasound probe (L50) was placed in the transverse-oblique plane at the level of the cricoid cartilage (C6) to obtain a cross-sectional view of the brachial plexus. Ultrasound imaging revealed the hypoechoic C5, C6, and C7 nerve roots located between the anterior scalene muscle and middle scalene muscle, lateral to the carotid artery and deep to the sternocleidomastoid muscle. Prior to needle insertion, 2 mL of 2% lidocaine was infiltrated subcutaneously at the puncture site to minimize discomfort. A 22 G, 80 mm insulated nerve block needle (Stimuplex® Ultra 360®, Braun, United States) was inserted using an in-plane technique from lateral to medial, advancing through the middle scalene muscle toward the lateral-posterior aspect of the C7 root. Hydrodissection was not routinely performed; needle position was confirmed via direct sonographic visualization of perineural spread. Once the needle tip was positioned adjacent to the nerve roots, 15 mL of a local anesthetic mixture (prepared by combining 10 mL of 0.5% bupivacaine and 10 mL of 2% lidocaine in a 1:1 ratio, resulting in final concentrations of 0.25% bupivacaine and 1% lidocaine) was injected slowly with intermittent aspiration. The spread of the anesthetic was visualized in real time, confirming correct perineural deposition (Fig. 2a).

Without withdrawing the needle from the skin after the interscalene block, a selective supraclavicular nerve block was subsequently performed. To achieve this, the ultrasound probe was moved cranially to visualize the superficial fascial plane immediately beneath the posterior border of the sternocleidomastoid muscle. The supraclavicular nerve was visualized as a thin hypoechoic structure located within the superficial fascial plane between the platysma and the middle scalene muscle. Using an in-plane technique, the same needle was redirected into this plane. After confirming the correct position, 5 mL of the previously described local anesthetic solution was slowly injected. The spread of the anesthetic and its perineural distribution were observed in real time under ultrasound guidance (Fig. 2b).

Following the block, sensory blockade was assessed approximately 15 minutes after the block, using pinprick testing over C4 – T1 dermatomes, yielding a score of 1 (no pain perception). Motor block was evaluated with a Modified Bromage score of ≥1. Surgery commenced approximately 30 minutes after the block application. The surgical procedure lasted 78 minutes in total, with no intraoperative complications. No additional sedatives or analgesics were required. Vital signs were monitored every five minutes, and hemodynamic stability was maintained throughout. No complications such as Horner's syndrome, phrenic nerve paralysis, respira-

tory depression, or total spinal anesthesia were observed. After surgery, the patient was transferred to the post-anesthesia care unit, where vital signs were monitored every 10 minutes for 30 minutes. At the time of transfer to the ward, her vital signs were: VAS 0/10, $SpO_2$ 98%, BP 124/77 mmHg, and pulse 92 bpm.

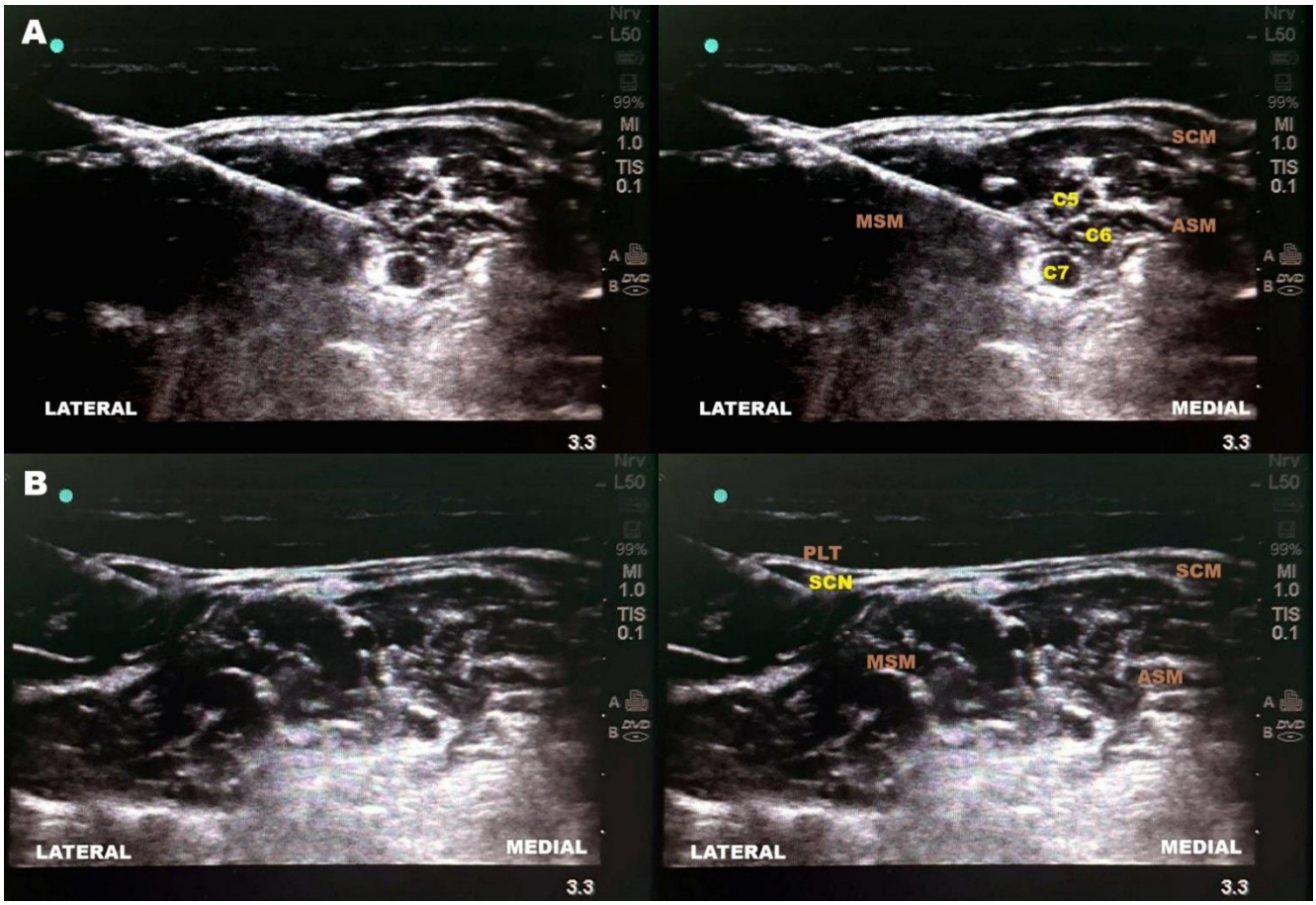


**Fig. 2.** (a) Ultrasound image obtained during interscalene block. The brachial plexus roots (C5, C6, C7) are visualized between the anterior scalene muscle (ASM) and middle scalene muscle (MSM). The in-plane needle is seen approaching from lateral to medial through the MSM.
(b) Ultrasound image during selective supraclavicular nerve block. The supraclavicular nerve (SCN) is seen within the fascial layer between the platysma (PLT) and the middle scalene muscle (MSM), targeted using an in-plane approach.

Approximately eight hours after the block, the patient experienced pain and mild paresthesia. Her pain was assessed as VAS 5. No preemptive or scheduled analgesics were administered as part of a multimodal analgesia regimen. Instead, 1 g of intravenous paracetamol was given only when the VAS score reached 5, resulting in a reduction to VAS 2. Pain control was successfully achieved, and no complications were observed during follow-up. Reassessment of fetal vital signs and ultrasonography results remained within normal limits. As the patient remained clinically stable, she was discharged with outpatient follow-up instructions.

## 3. Discussion

In this case, we describe the use of a combined interscalene and selective supraclavicular nerve block under ultrasound guidance in a patient at 32 weeks' gestation with clavicle fracture. The technique provided effective surgical anesthesia without the need for general anesthesia or intraoperative sedatives, and postoperative pain was managed with a single dose of paracetamol.

Trauma during pregnancy is a leading cause of maternal and fetal morbidity and mortality, with an incidence reported in approximately 6–7% of all pregnancies [1]. Trauma occurring in the third trimester is particularly concerning due to its association with severe perinatal outcomes, such as preterm labor, placental abruption, fetal distress, and fetal loss [5]. Therefore, a multidisciplinary approach that accounts for the physiological changes of pregnancy is essential in managing such high-risk cases.

In these scenarios, not only the effects of trauma but also the surgical and anesthetic management require close collaboration across specialties. In pregnant patients, general anesthesia must be approached with caution due to the increased risk of aspiration, decreased uteroplacental perfusion, and the potential teratogenic effects of pharmacologic agents crossing the placenta [6]. Physiological changes in the third trimester, such as airway edema, increased oxygen consumption, and de-

creased functional residual capacity, further increase the risks associated with general anesthesia [6]. Accordingly, regional anesthesia is often preferred when appropriate. Brachial plexus blocks, in particular, offer safe and effective analgesia while preserving consciousness [7].

In upper extremity surgeries, regional anesthesia not only provides adequate analgesia but also reduces the need for airway manipulation, thereby maintaining hemodynamic stability [8]. It has been shown that regional blocks can eliminate the need for conversion to general anesthesia while ensuring adequate surgical anesthesia throughout the procedure [9].

The sensory innervation of the clavicle is a complex network involving contributions from the supraclavicular, subclavian, long thoracic, and suprascapular nerves, making it one of the rare anatomical structures innervated by both the cervical and brachial plexuses [10]. Due to the complex neural innervation of the clavicular region, a single block technique is often insufficient, necessitating various combinations. Several regional techniques have been proposed for clavicle surgery, including supraclavicular plexus, interscalene, intermediate cervical plexus, costoclavicular, clavipectoral fascial plane, and PECS-Zero blocks [3,7,8,11,12]. The interscalene block acts by anesthetizing the roots of the brachial plexus (C5–C7) located between the anterior and middle scalene muscles. While effective for shoulder and clavicle surgery, this technique carries a risk of phrenic nerve blockade, which can result in ipsilateral hemidiaphragmatic paresis. Other possible complications include Horner's syndrome, vocal cord paralysis, spinal cord injury, and pneumothorax [3].

More recently, selective supraclavicular nerve blocks—targeting the more superficial supraclavicular nerve instead of the plexus—have gained importance. These blocks effectively anesthetize superficial tissues involved in clavicle surgeries using low volumes of local anesthetic, while reducing the risk of complications [4,13,14]. Moreover, they have been reported to reduce the incidence of complications such as hemidiaphragmatic paralysis [4]. Alternatively, a superficial cervical plexus block may also be used to anesthetize the supraclavicular nerves, offering a technically simpler and broader sensory coverage of the C3–C4 dermatomes [3]. However, the selective supraclavicular nerve block provides more focused anesthesia with potentially reduced risk of phrenic nerve involvement due to the smaller volume and limited spread, which may be particularly advantageous in pregnant or respiratory-compromised patients.

When combined with other brachial plexus blocks such as the interscalene block, selective supraclavicular nerve blocks administered with low volumes of local anesthetic can provide sufficient intraoperative analgesia and reduce postoperative analgesic requirements [14–16]. In the presented case, the combination of interscalene and selective supraclavicular nerve blocks resulted in effective surgical anesthesia. Motor blockade regressed within eight hours, and postoperative pain was controlled with paracetamol alone. These outcomes are consistent with findings from previous literature highlighting the effectiveness of regional techniques in pregnancy [16–18].

In pregnant patients, regional anesthesia avoids airway instrumentation, minimizes fetal drug exposure, and maintains hemodynamic stability. Lidocaine is classified as an FDA Pregnancy Category B drug, while bupivacaine is Category C due to animal studies indicating possible fetal risks [19]. However, both are commonly used in obstetric anesthesia at clinically appropriate doses. Regional techniques thus offer a safer alternative to general anesthesia in trauma-related surgeries during pregnancy. Numerous case reports have demonstrated the safety of regional blocks in pregnancy. For example, axillary brachial plexus blocks have been safely used in pregnant patients undergoing tendon repair during the second trimester, and popliteal sciatic nerve blocks have been successfully performed in the third trimester without complications [16,17]. Upper extremity surgeries under superior trunk blocks have also been completed without sedation [15]. Even when applied at anatomical sites distant from the uterus, regional anesthesia techniques have been reported to reduce fetal exposure and improve maternal-fetal safety outcomes [18].

This report has several limitations. As a single-patient experience, these findings may not be generalizable. Long-term follow-up data on maternal or fetal outcomes were not collected. In addition, the lack of comparative or objective outcome measures limits the strength of the conclusions.

## 4. Conclusions

This case highlights that the combination of an interscalene and selective supraclavicular nerve block can be a safe and effective anesthetic strategy for clavicle surgery in pregnancy. Especially in high-risk patients where general anesthesia poses significant concerns, ultrasound-guided regional anesthesia offers a viable alternative that minimizes fetal exposure, avoids airway manipulation, and ensures maternal hemodynamic stability. Increased awareness and dissemination of such targeted approaches may contribute to broader adoption of regional anesthesia in similar clinical scenarios and improve maternal-fetal outcomes in obstetric trauma care.

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***Data Availability***

*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

***Ethics Approval and Consent to Participate***

*Not applicable.*

***Author Contributions***

***Oguzhan Okumus:*** *conceptualization, methodology, investigation, writing – original draft, visualization.*
***Ahmet Ridvan Dogan:*** *supervision, validation, writing – review & editing.*
***Burcu Can:*** *data curation, literature review, writing – review & editing.*

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Challenge Journal of Perioperative Medicine

Case Report

# "Keeping it steady": Anaesthetic challenges in insulinoma surgery

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**ABSTRACT**

Insulinoma is a tumor of the pancreas that secretes excessive insulin, causing recurrent hypoglycemia. The median presentation age of 47 years and a mild female preponderance. Most cases are benign, with only 10% showing malignant potential. A typical presentation involves Whipple's triad, which includes symptomatic hypoglycemia, fasting blood glucose below 50 mg/dL, and immediate relief of symptoms after glucose administration. This case report discusses the perioperative anaesthetic management of a 54-year-old patient with insulinoma who underwent laparoscopic enucleation. A comprehensive approach involving preoperative blood glucose optimization through medications and dietary adjustments, vigilant intraoperative monitoring with timely dextrose infusion during tumor manipulation, and careful postoperative control of rebound hyperglycemia using insulin infusion is essential for improved outcomes in these patients. The primary treatment is surgical enucleation, but managing perioperative glycemic fluctuations presents significant challenges for anesthesiologists.

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## 1. Introduction

Insulinoma is a rare neuroendocrine tumor in the pancreas' islets of Langerhans causing excessive insulin production [1]. Most insulinomas are small and benign, with malignancy observed in only 10% of the cases [2]. Management typically involves surgical enucleation of the tumor, while malignant cases require both medical and surgical interventions [3]. Preoperative control of hypoglycemia and careful intraoperative monitoring are essential to avoid permanent neurological damage.

Managing such patient during perioperative period is challenging for anaesthesiologists. Normally, insulin secretion is tightly regulated by blood glucose concentration. In insulinoma, this regulation is lost - the tumor secretes insulin independently of blood glucose, Inhibition of Hepatic Gluconeogenesis and Glycogenolysis, Chronic hyperinsulinemia may blunt the physiological response of counter-regulatory hormones like glucagon and cortisol, making hypoglycemia episodes more severe and prolonged [4].

Treatment of hypoglycemia in insulinoma focuses on: Acute correction of hypoglycemia, Preoperative control of blood glucose, Definitive surgical removal of tumor.

Acute Treatment of Hypoglycemia: Dextrose Bolus: 50 mL of 50% dextrose (D50) IV bolus, Continuous Dextrose Infusion: D10W or D5W at a rate titrated to maintain normoglycemia, Frequent Blood Glucose Monitoring: Every 1–2 hours.

Definitive Treatment: Surgical Resection-Enucleation: For small, localized tumors (<2 cm), Distal pancreatectomy: If tumor is in body/tail, Whipple's procedure: For Pancreatic head tumors. Utilizing imaging modalities like CT, MRI, endoscopic ultrasonography, or calcium stimulation studies to accurately localize the tumor prior to surgery is crucial.

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## 2. Case Presentation

A 54-year-old male presented with episodes of fatigue, dizziness, restlessness, and recurrent hypoglycemia, occasionally resulting in loss of consciousness, relieved by dextrose administration. No significant medical or surgical history was reported, except for recent tobacco chewing. PET-CT (Positron emission tomography-computed tomography) with Ga-68 DOTA scan revealed a 3.7×2.7×3.2 cm necrotic, tracer-avid lesion at the superior margin of the pancreas, confirming insulinoma. A multidisciplinary approach was adopted. Involving anesthesiologist, surgeon, and endocrinologist. A plan was proposed to surgically excise the tumor after taking patient written consent. We have also obtained written consent from the patient to present and publish this case. Laboratory investigations of the patient are given in Table 1.

**Table 1.** Blood chemistry of the patient.

| Factor | Patient values | Normal range |
|---|---|---|
| Cortisol | 13.53mcg/dl | 5.2-35mcg/dl. |
| Fasting insulin level | 13.10mU/L | 2-25Mu/dl |
| C PEPTIDE | 4.42ng/ml | 1.1-4.4ng/ml. |
| D-3-Hdroxybutyrate(ketone) | 0.10mmol/L | 0.02-0.27 |
| Prolactin | 8.696ng/ml. | Male-1.99-19.40ng/ml |

The patient was admitted for glucose monitoring and optimization. During observation, symptomatic hypoglycemia (45 mg/dL) was managed with intravenous glucose. Pre-anaesthesia assessment revealed normal vital signs, airway examination (Modified Mallampati Grade II), and good effort tolerance. The patient's BMI was 29.06 kg/$m^2$.

To minimize fasting-related hypoglycemia, clear glucose-containing liquids were allowed up to two hours before surgery, and 10% dextrose was infused at 50 mL/h intravenously during the fasting period.

The patient was transferred to the operating room (OR) and standard ASA (American Society of Anaesthesiology) monitors attached. An epidural catheter was secured at the L1-L2 inter-space. Premedication with Injection ondansetron 4 mg iv, Injection glycopyrrolate 0.2 mg iv, and Injection Midazolam 2 mg iv was given, Injection fentanyl 100mcg iv was given after premedication. Patient was induced with Injection propofol 100 mg iv, and Injection. Vecuronium 8 mg iv, followed by endotracheal intubation with 7.5 sized ET tube. Oxygen:$N_2O$ (50:50) and Isoflurane was used for maintenance of anaesthesia intraoperatively. Blood glucose was monitored every 30 minutes during surgery, the Graph 1 below depicts the intraoperative trends of GRBS (General random blood sugar) levels over time. Effect of increased abdominal pressure on cortisol release and disturbance in glucose metabolism was discussed with surgeon. Intra-abdominal pressure changes and its effects on the tumor was also discussed and was kept at minimal 10–12 mmHg throughout the procedure to minimize the effect of Intra-abdominal pressure on glucose metabolism. A firm, nodular mass (3×4 cm) was successfully excised from the proximal pancreatic body. Prior to removal of tumor dextrose containing fluids were used as maintenance fluid to avoid hypoglycemia during tumor handling. After tumor resection, dextrose infusion was replaced with normal saline (100 mL/h). Intra-operative glucose levels remained within normal limit and has been plotted in Fig. 1 and the patient's hemodynamics were well-controlled throughout the five-hour surgery. Reversal of neuromuscular blockade was done using Injection Sugammadex (190 mg) iv, and the patient was extubated uneventfully.

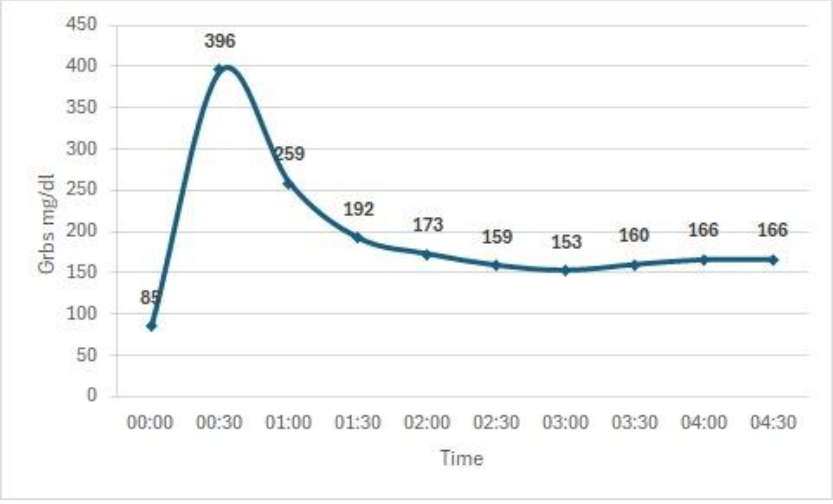


**Fig. 1.** Blood sugar level checked half hourly (GRBS: General random blood sugar in mg/dl).

The patient was transferred to the PACU and NS infusion at 1–2 mL/kg/h was continued for four hours. Blood glucose levels were checked 4th hourly, which remained stable initially but rose above 200 mg/dL on postoperative day 1. Regular insulin was initiated according to sliding scale to maintain glucose levels between 100–150 mg/dL. Insulin therapy was discontinued by postoperative day 7, with the patient maintaining normal glucose levels. He was discharged on postoperative day 9 with advice for regular glucose monitoring at home (Fig. 2).

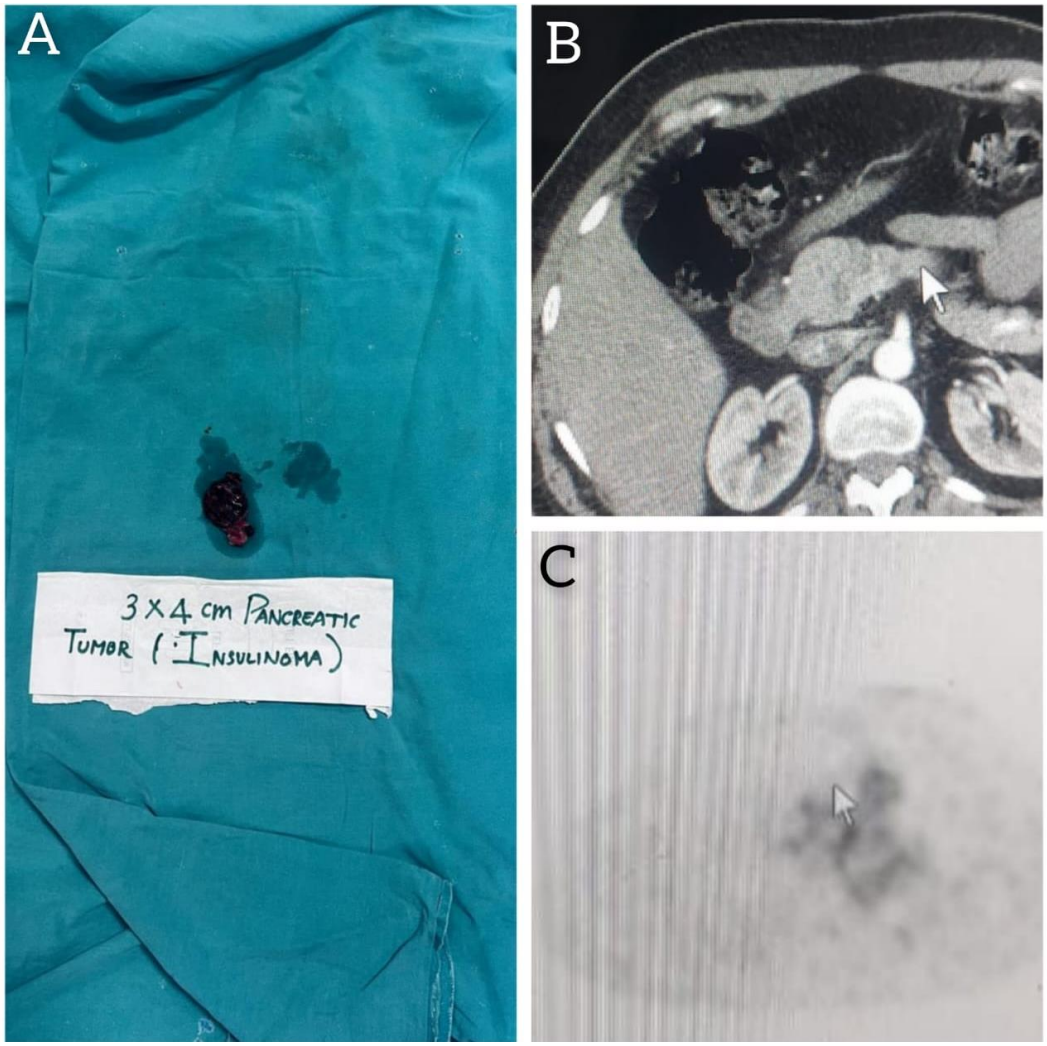


**Fig. 2.** (a) Excised pancreatic tumor (insulinoma); (b) CECT (Contrast enhanced computed tomography) abdomen showing solitary nodule in tail of pancreas near hilum of spleen (white arrow); (c) PET scan of insulinoma.

## 3. Discussion

Insulinoma is the most common cause of endogenous hyperinsulinism, presenting with Whipple's Triad: neuroglycopenic symptoms (e.g., confusion, agitation) and rapid symptom relief with glucose administration [2,5–7]. Diagnosis may be delayed or misinterpreted as a psychiatric or neurological disorder. A supervised 72-hour fasting test, demonstrating inappropriately high insulin (≥6 U/mL) and C-peptide levels (≥0.2 nmol/L), remains the gold standard for diagnosis [2].

While surgical enucleation is the definitive treatment, perioperative glycemic control is crucial to prevent hypoglycemic episodes that could lead to neuronal injury [3]. Monitoring glucose every 15–30 minutes intraoperatively is recommended as signs of hypoglycemia are masked under general anaesthesia [4]. Here we closely monitored the perioperative glucose levels throughout the procedure, adjusting the fluids administration based on GRBS readings. Propofol is preferred for induction as it maintains stable insulin-glucose homeostasis, Halothane and Enflurane are avoided due to the fact that they influence insulin sensitivity [4].

Here we used propofol for induction as it helps maintain stable insulin glucose homeostasis during the perioperative period. Elevated intra-abdominal pressure during laparoscopic procedures can trigger cortisol release, complicating glucose control [8]. Even though laparoscopic enucleation was done in our case, we discussed the risk of cortisol release on increasing intra-abdominal pressure and disturbance in glucose metabolism intra operatively with the surgeon, and intra-abdominal pressure was kept to a minimum of 10–12 mmHg throughout the procedure [8]. Immediate normalization of insulin levels post-resection is a strong indicator of successful surgery [9,10]. Usually insulin levels come to

normal level 20 minutes post-surgery, but may take 2–3 days. In our case there were no hypoglycemic episodes seen post resection and post operatively, indicating normalization of insulin secretion post enucleation [1]. Monitoring of sugars in post-operative period every 4th hourly is recommended to avoid hypoglycemic episodes.

The long-term prognosis of insulinoma depends on complete resection, with cure rates between 75–98% [2]. Patients with multiple endocrine neoplasia type 1 (MEN 1) have higher recurrence [6].

Incidence of insulinoma is exceedingly rare, and perioperative management of sugars and hypoglycemia is challenge for anaesthesiologists.

In our case, we administered general anaesthesia in combination with thoracic epidural analgesia, which aligns with many reported practices but also offers distinct advantages. While the literature often emphasizes general anaesthesia alone or with peripheral blocks such as transversus abdominis plane (TAP) blocks for laparoscopic procedures, our approach prioritized superior visceral analgesia, intraoperative hemodynamic stability, and optimal postoperative pain control. The thoracic epidural allowed us to reduce intraoperative opioid use and improve bowel recovery, which are critical considerations in abdominal surgeries. Alternative anesthetic techniques could include total intravenous anaesthesia (TIVA) using propofol and remifentanil, especially in patients with increased risk of postoperative nausea or requiring neuromonitoring. For regional alternatives, nerve blocks like TAP or rectus sheath blocks may be considered, particularly when epidural is contraindicated. Regarding postoperative analgesia, a multimodal regimen including paracetamol, NSAIDs (where not contraindicated), and continued epidural infusion (or local infiltration if epidural is not feasible), interfacial plane blocks like Erector Spinae Plane block, TAP block, QL (Quadratus lumborum) block can provide effective pain relief while minimizing opioid-related side effects. Multimodal analgesia can certainly incorporate regional techniques enhancing recovery and reducing complications. Our method, therefore, reflects a balanced, patient-tailored strategy emphasizing hemodynamic control, effective analgesia, and early mobilization, thereby early recovery and discharge of patient.

## 4. Conclusions

Anesthetic management of insulinoma requires strict perioperative glycemic control to prevent both hypoglycemia and hyperglycemia. In this case, meticulous intraoperative glucose monitoring and timely postoperative insulin therapy led to a smooth recovery. Close-loop communication between the anaesthesia and surgical teams was vital during tumor handling. Surgical resection remains the definitive treatment with good outcomes when complete excision is achieved. Vigilant monitoring helped prevent hypoglycemia and potential neurological damage. Given the rarity of such cases, we documented this report to highlight the importance of tight glucose control and effective interdisciplinary coordination in the anesthetic management of insulinoma.

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***Data Availability***
*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

***Ethics Approval and Consent to Participate***
*Not applicable.*

***Author Contributions***
***Prakash Muralidhar Padamukhe:*** *conceptualization, methodology, investigation, writing – original draft, supervision.*
***Swetha R. Gowda:*** *literature review, writing – review & editing.*
***Siri Chandana Kanamarlapudi:*** *visualization, validation, data curation.*
***Pragna Hospet:*** *formal analysis, perioperative monitoring, writing – review & editing.*

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Challenge Journal of Perioperative Medicine

**Letter to the Editor**

# Motor block following lumbar erector spinae plane block for postoperative analgesia after lumbar spinal surgery: A case report

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Dear Editors,

Postoperative pain remains a challenge following lumbar disc herniation surgery [1]. Erector spinae plane block (ESPB) entails the injection of a local anesthetic into the deep fascia of the erector spinae muscle. It can be administered from the cervical to sacral levels and is regarded as safe due to its clear visualization and anatomical distance from critical structures such as the pleura [2]. However, case reports suggest that ESPB may induce unexpected motor block due to paravertebral spread [3].

This case report describes a patient who developed motor block after a lumbar ESPB for postoperative analgesia following lumbar disc herniation surgery.

A 32-year-old female (99 kg, 170 cm, ASA II) presented with right lower back, hip, and leg pain, accompanied by numbness in the right leg, and underwent a right L4-L5 microdiscectomy without intraoperative complications. Thirty minutes before extubation, the patient received 1 g of paracetamol and 100 mg of tramadol for analgesia. Additionally, a bilateral erector spinae plane block (ESPB) was performed at the L4-L5 level using a convex transducer placed 4 cm lateral to the midline in the sagittal plane. After confirming needle placement at the L4 transverse process with 5 ml of 0.9% NaCl, 30 ml of 0.25% bupivacaine was administered bilaterally (total of 60 ml).

Postoperatively, neurological examination revealed a complete motor block (Bromage score of 3) in the left lower extremity. This motor block was suspected to result from paravertebral spread of the ESPB; however, a lumbar MRI was performed to exclude complications such as hematoma. Imaging revealed no hematoma, infection, spinal cord or nerve root compression, or other surgical complications. Motor function gradually improved within 12-16 hours, and the patient regained movement in the left lower extremity. After symptomatic improvement, the patient was discharged with follow-up recommendations in the neurosurgery clinic.

ESPB may enhance local anesthetic spread near dorsal and ventral roots, covering lateral cutaneous branches and rami communicantes. Cadaveric studies show cranio-caudal contrast spread from T2 to L3 (right) and C5 to L2 (left) at T7, with radiological evidence from C7 to T8 at T5 and cold sensation loss from T5 to L2 at T8, suggesting effective visceral and somatic pain control [3]. The enhanced analgesic effect of ESPB may result from wound infiltration, increased vascular absorption in the highly vascularized erector spinae muscle, or epidural spread facilitated by anatomical disruptions from laminectomy. These mechanisms, individually or combined, may explain its effectiveness in this surgical context [4].

High-volume, high-concentration local anesthetics may induce motor side effects, including bilateral sensory block after unilateral ESPB [3,5]. In this case, a higher volume was administered for effective pain control, though it may have contributed to motor block.

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Various techniques, including modified thoracolumbar interfascial plane (m-TLIP) and Quadro Iliac Plane Block (QIPB), are used for pain control after lumbar surgery. Ciftci et al. [1] found no significant difference in intra- and postoperative pain management between ESPB and mTLIP in lumbar spine surgery. Tulgar et al. [6] introduced the QIPB for hip, lower abdominal, and lumbosacral surgeries, which may offer advantages in lumbar procedures due to its distance from the surgical field and broad distribution.

This case report provides a detailed account of motor block following ESPB. Clinicians may choose different regional anesthesia techniques for postoperative pain management in lumbar spinal surgery based on their experience.

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***Data Availability***

*The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.*

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*Written informed consent was obtained from the participants. All methods were performed in accordance with relevant guidelines and regulations.*

***Author Contributions***

***Hande Gungor:*** *conceptualization, investigation, writing – original draft, visualization.*
***Ahmet Cetinkal:*** *clinical supervision, validation, writing – review & editing.*

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