

e-ISSN: 3023-6738

Eurasian Journal of

Anesthesiology & Intensive Care

Volume: 2

Issue: 1

Year: 2025



EAJAIC



MHA
MEDIHEALTH ACADEMY

Eurasian Journal of
Anesthesiology & Intensive Care
Editorial Board

EDITOR-IN-CHIEF

Assoc. Prof. Musa ZENGİN

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

ASSOCIATE EDITORS-IN-CHIEF

Prof. Ali ALAGÖZ

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Assoc. Prof. Fatma KAVAK AKELMA

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Yıldırım Beyazıt University, Ankara, Türkiye

Assoc. Prof. Savaş ALTINSOY

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

EDITORIAL BOARD

Assoc. Prof. Alparslan KOÇ

Department of Anesthesiology and Reanimation, Mengücek Gazi Training and Research Hospital, Faculty of Medicine, Erzincan Binali Yıldırım University, Erzincan, Türkiye

Asst. Prof. Burak NALBANT

Department of Anesthesiology and Reanimation, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye

Assoc. Prof. Ceyda ÖZHAN ÇAPARLAR

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Prof. Derya ÖZKAN

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Assoc. Prof. Emine ARIK

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Assoc. Prof. Emine Nilgün ZENGİN

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Türkiye

Prof. Erkan Yavuz AKÇABOY

Department of Algology, Ankara Bilkent City Hospital, Ankara, Türkiye

Assoc. Prof. Gülsen KESKİN

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Assoc. Prof. Gülten ÜTEBEY

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Assoc. Prof. Güvenç DOĞAN

Department of Anesthesiology and Reanimation, Faculty of Medicine, Hitit University, Çorum, Türkiye

Spec. Hülya YİĞİT

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Türkiye

Assoc. Prof. İlkey Baran AKKUŞ

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Eurasian Journal of
Anesthesiology & Intensive Care
Editorial Board

Assist. Prof. Mehmet ŞAHAP

Department of Anesthesiology and Reanimation, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye

Prof. Mehmet Murat SAYIN

Division of Intensive Care, Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Assoc. Prof. Münire BABAYİĞİT

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Prof. Nevriye SALMAN

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Türkiye

Assoc. Prof. Nevzat Mehmet MUTLU

Department of Intensive Care, Ankara Bilkent City Hospital, Ankara, Türkiye

Assoc. Prof. Onur KARACA

Department of Anesthesiology and Reanimation, Faculty of Medicine, Aksaray University, Aksaray, Türkiye

Assoc. Prof. Ramazan BALDEMİR

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Assoc. Prof. Selçuk KAYIR

Department of Anesthesiology and Reanimation, Faculty of Medicine, Hitit University, Çorum, Türkiye

Assoc. Prof. Semih BAŞKAN

Department of Anesthesiology and Reanimation, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye

Assoc. Prof. Semih AYDEMİR

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Prof. Taylan AKKAYA

Department of Algology, Ankara Bilkent City Hospital, Ankara, Türkiye

Spec. Yusuf ÖZGÜNER, MD

Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

Prof. Zeliha Aslı DEMİR

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Türkiye

Prof. Zeynep Nur AKÇABOY

Department of Anesthesiology and Reanimation, Ankara Bilkent City Hospital, Ankara, Türkiye

ENGLISH LANGUAGE EDITOR

Assoc. Prof. Esra Güzel TANOĞLU

Department of Molecular Biology and Genetics, Institute of Health Sciences, University of Health Sciences, İstanbul, Türkiye

STATISTICS EDITOR

Spec. Onur KÜÇÜK, MD

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

LAYOUT EDITOR

Hatice AKYIL

Biologist, MediHealth Academy Publishing, Ankara, Türkiye

Eurasian Journal of
Anesthesiology & Intensive Care
Editorial

Dear Colleagues,

We are pleased to announce the release of the second-year first issue of The Eurasian Journal of Anesthesiology and Intensive Care (EAJAIC), under the auspices of Medihealth Academy, in February 2025. We extend our gratitude to all researchers, referees, and members of the editorial board who contributed to the preparation of the journal. Additionally, we express our thanks to the printing team for their efforts in bringing it to publication. In our first issue this year, we are delighted to present five original research articles and two review articles. Moving forward, with your support, our goal is to have EAJAIC recognized in national and international scientific indexes. I would like to express my sincere gratitude for all the support and interest you have shown.

Best regards,

Assoc. Prof. Musa ZENGİN
Editor in Chief

Eurasian Journal of
Anesthesiology & Intensive Care
Contents

Volume: 2 Issue: 1 Year: 2025

ORIGINAL ARTICLES

- From anesthesia to healing: the potential of topical sevoflurane in enhancing wound repair 1-6
Çelik E, Arslankoz S, Koyuncu P, Ögüş E, Polat R, Dönmez A.
- Comparison of interleukin-6 receptor antagonist and pulse steroid therapy in critically ill patients with COVID-19: retrospective analysis 7-11
Koç F, Babayiğit M, Babayiğit MA, Menteş O, Fırat Göktaş E, Dereli N.
- Assessment of YouTube videos on ultrasound-guided lower extremity peripheral nerve blocks 12-17
Göger E.
- Examining the effects of lidocaine and dexmedetomidine on compound action potential in rat sciatic nerve 18-23
Toprak H, Öztin Ögün C.
- Retrospective investigation of cases diagnosed with brain death..... 24-28
Bayrakçı S, Eygi E.

REVIEWS

- Traditional and complementary medicine practices in postoperative analgesia..... 29-34
Babayiğit M, Babayiğit MA, Koşar B.
- Anesthesia for urological procedures 35-39
Türksal E.

From anesthesia to healing: the potential of topical sevoflurane in enhancing wound repair

 Erdi Çelik¹,  Sehbal Arslankoz²,  Pinar Koyuncu³,  Elmas Ögüş³,  Reyhan Polat¹,  Aslı Dönmez¹

¹Department of Anesthesiology and Reanimation, Ankara Etlik City Hospital, Ankara, Türkiye

²Department of Pathology, Ankara Etlik City Hospital, Ankara, Türkiye

³Department of Biochemistry, Ankara Etlik City Hospital, Ankara, Türkiye

Cite this article: Çelik E, Arslankoz S, Koyuncu P, Ögüş E, Polat R, Dönmez A. From anesthesia to healing: the potential of topical sevoflurane in enhancing wound repair. *Eur J Anesthesiol Intens Care*. 2025;2(1):1-6.

Corresponding Author: Aslı Dönmez, aslidonmez@hotmail.com

Received: 01/10/2024

Accepted: 04/11/2024

Published: 03/02/2025

ABSTRACT

Aims: Sevoflurane is a volatile anesthetic agent commonly used for the induction and maintenance of general anesthesia. Recent case reports and case series have highlighted the analgesic and anti-inflammatory properties of sevoflurane when applied topically to venous ulcers, diabetic wounds, and infected wounds. This study investigates the therapeutic effects of topically applied sevoflurane on thermal burn wounds in rats, focusing on inflammatory responses and wound healing processes.

Methods: Twenty-one male Wistar Albino rats underwent the induction of a second-degree thermal burn covering 3 cm² on the interscapular skin. The animals were randomized into three groups: the experimental group (group S) received 3 ml of topical sevoflurane (1 ml/cm²), the control group (group I) received 3 ml of isotonic saline, and the sham group (group K) received no treatment. Plasma concentrations of TNF- α , IL-1 β , IL-6, and IL-10 were measured at baseline, and on days 7 and 14 post-injury. Histopathological evaluations of the burn sites were conducted on day 14, assessing for active and chronic inflammation, granulation, and fibrosis.

Results: All rats in the study maintained similar age and weight profiles across the groups. Histologically, the sevoflurane group exhibited significantly reduced chronic inflammation and enhanced granulation and fibrosis compared to controls. Immunologically, IL-6 and IL-10 levels were elevated in the isotonic group but did not differ significantly from baseline in other groups. Plasma cytokine levels were comparable across all groups.

Conclusion: Topical sevoflurane appears to promote wound healing by modulating inflammatory responses and enhancing tissue repair processes in a rat burn model. These findings indicate that sevoflurane may serve as a beneficial adjunctive therapy in the management of burn injuries and general wound care. Given its established anti-inflammatory effects when inhaled, there is a compelling need for further research to investigate the potential benefits and mechanisms of topical sevoflurane application. Such studies could provide valuable insights into optimizing wound healing processes and improving patient outcomes.

Keywords: Inflammation, sevoflurane, topical application, wound healing

INTRODUCTION

Sevoflurane is a volatile anesthetic agent commonly used for the induction and maintenance of general anesthesia. Recent literature has reported its potential as a topical treatment for venous ulcers, diabetic wounds, and infected wounds, demonstrating analgesic and anti-inflammatory effects that contribute to wound healing.¹⁻³

Although the exact anti-inflammatory mechanisms of sevoflurane are not fully elucidated, hypotheses suggest it may

modulate pro-inflammatory cytokine levels and stimulate anti-inflammatory pathways, particularly influencing IL-10 production.⁴⁻⁶ Despite anecdotal evidence supporting topical sevoflurane's efficacy in analgesia and wound repair, a gap remains in clinical research regarding its healing effects. Wound healing is a complex process, critically involving inflammatory cell migration and signaling molecule expression, which are integral to tissue restoration following injury.⁷

This study aims to explore the impact of topical sevoflurane on wound healing by evaluating histopathological and immunochemical responses in a controlled rat model.

We hypothesize that the topical application of sevoflurane will significantly improve wound healing in a rat thermal burn model. This improvement is theorized to manifest through a quantifiable reduction in chronic inflammation and an increase in granulation tissue and fibrosis, as observed in histopathological evaluations. Furthermore, we posit that sevoflurane will modulate the expression of key immunochemical markers, including pro-inflammatory and anti-inflammatory cytokines, contributing to the complex physiological process of tissue repair and integrity restoration post-injury.

METHODS

Approval for this investigation was obtained from the Animal Experiments Local Ethics Committee of Ankara Training and Research Hospital (Date: 26.11.2020, Decision No: 0063-646). The study was undertaken at the Animal Research Centre of Ankara Training and Research Hospital and was financially supported by the Scientific Research Projects Coordination Unit of Health Sciences University Dışkapı Yıldırım Beyazıt Health Applications and Research Centre (BAP No: 78/03). We included 21 male Wistar albino rats, aged between 10-12 weeks, each weighing 250-300 grams. The subjects were randomly assigned into three distinct groups, identifiable by numbered tail labels, and comprised of the experimental group (group S, n=7), the control group (group I, n=7), and the sham group (group K, n=7). All rats were anesthetized with an intramuscular injection of 50 mg/kg ketamine (Ketalar flacon, Pfizer Pharma GMBH, Germany) and 10 mg/kg xylazine hydrochloride (Alfazyne 2%, Alfasan International, Holland). The back region of each rat was shaved, and a second-degree thermal burn measuring 3 cm² was induced on the shaved interscapular region using a heated metal plate. Group S received a topical dose of 3 ml (1 ml/cm²) sevoflurane (Sevorane 100% 250 ml. solution, Abbvie Laboratories, IL, USA) applied as a liquid to the burn area. Sponges soaked with sevoflurane were held on the wound by the practitioner's gloved hand until the sevoflurane evaporated or the rats' respiratory patterns were disrupted by the evaporating sevoflurane. Group I received the same volume of isotonic saline, and group K received no intervention. Wound care was repeated every other day.

All rats were maintained under veterinary supervision for 14 days in the same environment, with identical food and water, in temperature-controlled cages with a 12-hour light-dark cycle. No antibiotics were administered to the rats at any time, and there were no animal losses during this period.

Intracardiac blood samples were collected from all rats on days 0, 7, and 14. These blood samples were centrifuged at 3500 rpm for 10 minutes, and serum was separated and stored at -80°C until analysis. IL-1 β , IL-6, IL-10, and TNF- α concentrations in the serum samples were analyzed using the Enzyme linked immunosorbent assay (ELISA) method (USCN, Wuhan, Hubei, PRC). Optical density (OD) measurements were taken for samples bound with biotinylated antibodies using an EL-800 ELISA reader, and cytokine concentrations were determined by comparing the OD of the samples with the OD curve of a standard sample.

On the 14th day, after deep anesthesia, the rats were sacrificed through intracardiac exsanguination and biopsy samples were obtained from the incision line, forming 2x2 cm² strips that included healthy tissue. After fixation in formalin, routine tissue processing was applied to all samples, and paraffin blocks were prepared. Two slices, each 4-5 μ m in thickness, were sectioned from the paraffin blocks. One slice was stained with hematoxylin eosin (HE), and the other with Masson's trichrome stain (BESLAB, Histo-Med, Ankara, Turkey).

Additionally, on the tenth day, tissue samples were also scored for histopathological evaluation, including active inflammation, chronic inflammation, granulation tissue, and fibrosis, scored using a semi-quantitative method (0: none, 1: mild, 2: moderate, 3: severe).

The HE-stained slices were evaluated for active inflammation, chronic inflammation, and granulation tissue formation, while the Masson's trichrome-stained slices were assessed for fibrosis. The severity of acute and chronic inflammation was determined by roughly counting the proportion of neutrophil leukocytes for acute inflammation and mature lymphocytes and plasma cells for chronic inflammation observed in a high-power field. The formation of granulation tissue was evaluated according to the intensity of small vessel proliferation observed in a high magnification field. Fibrosis was graded according to fibroblastic activity beneath the wound tissue and collagenization. All parameters were scored semi-quantitatively as follows: 0 (none), 1 (mild), 2 (moderate), and 3 (severe). For acute inflammation: 0 (none): neutrophil leukocyte <5; 1 (mild): 10-50 neutrophils leukocytes; 2 (moderate): >50 neutrophils; 3 (severe): abscess formation or plate-forming neutrophil leukocyte observation. For chronic inflammation: 0 (none): <5 mature lymphocytes or plasma cells; 1 (mild): 5-50 mature lymphocytes or plasma cells; 2 (moderate): clustered mature lymphocytes and/or plasma cells; 3 (severe): diffuse infiltration of mature lymphocytes and/or plasma cells. Granulation tissue: 0 (none): no small vessel proliferation; 1 (mild): a few congested small vessel proliferations that do not form clusters in one high power field; 2 (moderate): proliferation of several small vessels arranged back-to-back in a high magnification field; 3 (severe): numerous small-diameter vascular structures in one high-power field. Fibrosis: 0 (none): No trichome staining was observed; 1 (mild): presence of sparse thin collagen fibers; 2 (moderate): the presence of collagen fibers that are coarsened but do not form bundles; 3 (severe): presence of coarse collagen fibers in bundles. Stained sections were examined independently by two pathologists.

Statistical Analysis

The data analysis was performed using SPSS for Windows version 21.0 software (Statistical Package for Social Sciences). Data did not conform to a normal distribution based on the Shapiro-Wilk test. Descriptive statistics are presented as median and interquartile range (IQR) values for continuous variables. Kruskal-Wallis test was applied for comparisons among the experiment, control, and sham groups, Friedman test for within-group comparisons, and ANOVA for the evaluation of all groups in repeated measurements. The Fisher Exact test was used for the comparison of categorical variables. A 95% confidence interval was used for result evaluation, and a p-value less than 0.05 was considered statistically significant in all analyses.

RESULTS

All rats in the study maintained similar age and weight profiles across the groups.

The histopathological findings of the groups and the distribution of inflammation severity are shown in [Table 1](#). When statistical evaluations were made between the groups in terms of active inflammation, chronic inflammation, granulation, and fibrosis ([Table 2](#)), a difference in the severity of active inflammation was noted between the experimental, control, and sham groups, but it was not statistically significant ($p>0.05$). The severity of chronic inflammation was significantly lower in the sevoflurane group compared to the other two groups ($p=0.011$). Severe chronic inflammation was observed in 2 subjects in the sham group but was absent in the sevoflurane and isotonic groups. Mild chronic inflammation was observed in 6 subjects in the sevoflurane group, 2 subjects in the isotonic group, and 5 subjects in the sham group ([Figure 1](#)).

Granulation severity was significantly higher in the sevoflurane group compared to the other two groups ($p=0.005$). Severe granulation findings were observed in 4 subjects in the sevoflurane group, but none in the isotonic and sham groups. Mild granulation findings were observed in 4 subjects in the sham group and 1 subject in the isotonic group; no mild granulation was observed in the sevoflurane group ([Figure 2](#)).

Fibrosis severity was significantly higher in the sevoflurane group compared to the other two groups ($p=0.018$). Severe fibrosis findings were found in 5 subjects in the sevoflurane group, and in one subject each in the isotonic and sham groups. Mild fibrosis was observed in 1 subject in the sevoflurane group, 3 subjects in the isotonic group, and 6 subjects in the sham group ([Figure 3](#)).

When examining median (IQR) values, descriptive statistics, and comparative analyses for TNF- α , no statistically significant differences were found between the experimental, control, and

Table 1. Comparative analysis of plasma TNF- α , IL-1 β , IL-6, IL-10 levels

	Sham (n=7)	Isotonic (n=7)	Sevoflurane (n=7)	p*	p**
TNF- α (day 0) (pg/ml)	26.40 (76.32)	80.84 (73.00)	104.92 (198.28)	0.301	
TNF- α (day 7) (pg/ml)	116.16 (131.52)	225.92 (214.60)	160.86 (343.04)	0.572	0.732
TNF- α (day 14) (pg/ml)	133.14 (113.36)	157.60 (52.78)	141.30 (117.68)	0.925	
p***	0.066	0.156	0.867		
IL-1 β (day 0) (pg/ml)	7.12 (5.10)	9.16 (7.46)	5.08 (3.40)	0.291	
IL-1 β (7.gün) (pg/ml)	8.14 (3.72)	9.48 (10.18)	9.16 (4.08)	0.476	0.738
IL-1 β (day 14) (pg/ml)	7.80 (3.06)	6.78 (2.38)	8.82 (7.46)	0.477	
p***	0.368	0.158	0.156		
IL-6 (day 0) (pg/ml)	4.26 (5.20)	4.72 (1.76)	4.26 (8.52)	0.687	
IL-6 (day 7) (pg/ml)	6.14 (5.44)	8.52 (2.58)	5.78 (1.56)	0.279	0.380
IL-6 (day 14) (pg/ml)	6.14 (3.08)	6.86 (2.60)	6.14 (4.02)	0.762	
p***	0.368	0.012	0.867		
IL-10 (day 0) (pg/ml)	9.30 (0.00)	5.32 (7.98)	8.62 (5.98)	0.386	
IL-10 (day 7) (pg/ml)	11.94 (7.94)	15.92 (13.94)	14.60 (13.94)	0.360	0.691
IL-10 (day 14) (pg/ml)	15.26 (27.40)	19.26 (13.26)	24.56 (25.10)	0.669	
p***	0.254	0.021	0.180		

Descriptive statistics were stated as median (IQR), p*: Intergroup comparisons over the same time period, p**: Intergroup comparisons across all time periods, p***: Within-group comparisons across all time periods

Table 2. Distribution and degree of histopathological findings

	Active inflammation	Chronic inflammation	Granulation	Fibrosis
Sham (n=7)				
K1	1	3	2	1
K2	2	1	1	1
K3	3	3	1	3
K4	3	1	2	1
K5	2	1	1	1
K6	3	1	1	1
K7	2	1	2	1
Isotonic (n=7)				
I1	1	2	2	2
I2	2	1	1	1
I3	2	2	2	3
I4	1	2	2	2
I5	3	1	2	1
I6	2	2	2	1
I7	1	2	2	2
Sevoflurane (n=7)				
S1	2	1	2	3
S2	1	1	3	3
S3	3	1	2	3
S4	3	1	3	3
S5	1	1	2	3
S6	3	2	3	2
S7	1	1	3	1

K: Sham group, I: Isotonic group, S: Sevoflurane group Histopathological evaluation: 0=none, 1=mild, 2=moderate, 3=severe

sham groups at any time points examined ($p>0.05$). For IL-1 β , no statistically significant differences were detected between the experimental, control, and sham groups at any time points examined ($p>0.05$). For IL-6, a statistically significant difference was observed in the isotonic group at the 14-day mark ($p=0.012$), but no significant changes were noted in IL-6 levels in the sham and sevoflurane groups ($p>0.05$). For IL-10, a statistically significant difference was found in the isotonic group at the 14-day mark ($p=0.021$), while no significant changes were noted in IL-10 levels in the sham and sevoflurane groups ($p > 0.05$) ([Table 3](#)).

DISCUSSION

The results of this study demonstrate that topical application of sevoflurane on thermal burn wounds in a rat model has a positive impact on wound healing. This impact is characterized by a reduction in chronic inflammation and an increase in granulation and fibrosis, as observed in the histopathological evaluation. However, there were no significant changes in the plasma levels of IL-6, IL-8, IL-10, and TNF- α when measured immunochemically.

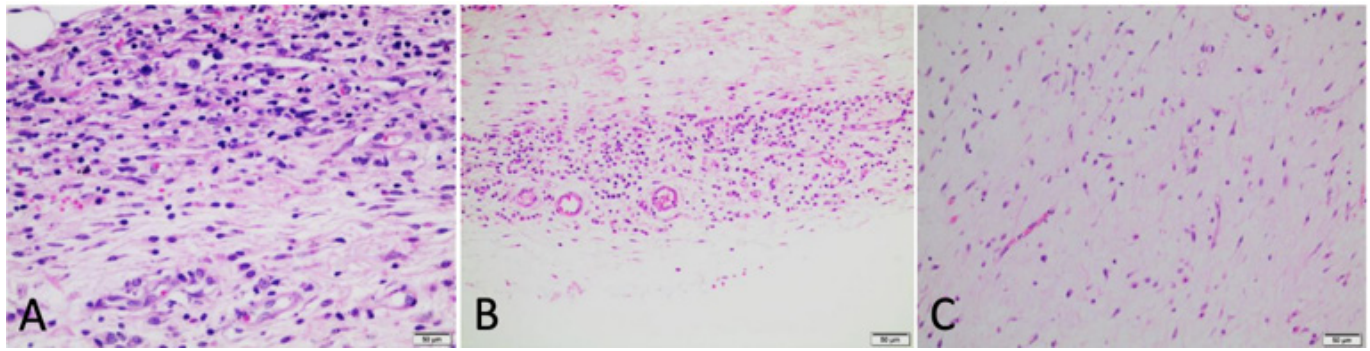


Figure 1. Histopathological evaluation of chronic inflammation, **A.** Severe chronic inflammation (H&E X200) observed in the Sham group. **B.** Severe chronic inflammation at the wound base in group I (H&E X200). **C.** Mild chronic inflammation noted in group S (H&E X200).

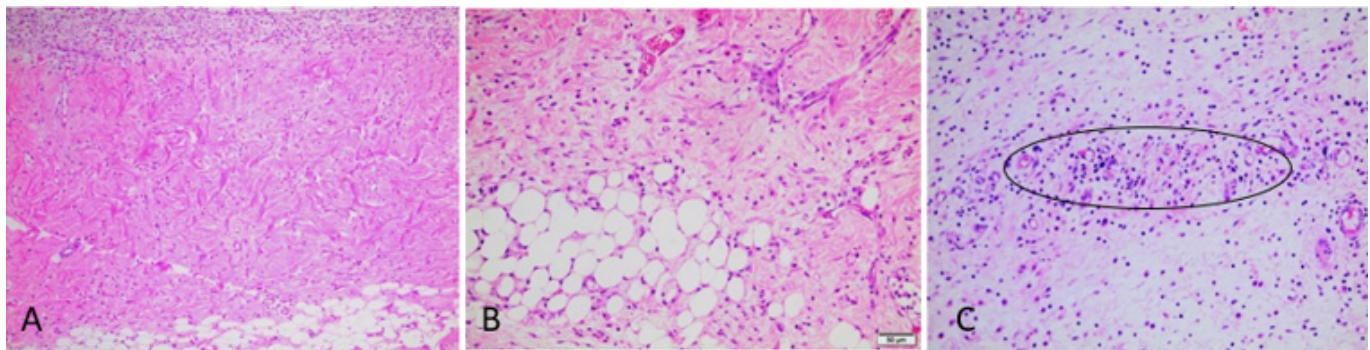


Figure 2. Analysis of granulation tissue formation, **A.** Signs of chronic inflammation in the upper part of the image with no granulation tissue development in group 0 (H&E X200). **B.** Chronic inflammation at the wound base without granulation tissue formation in group I (H&E X200). **C.** Proliferating vascular structures indicating granulation tissue in group S (H&E X200).

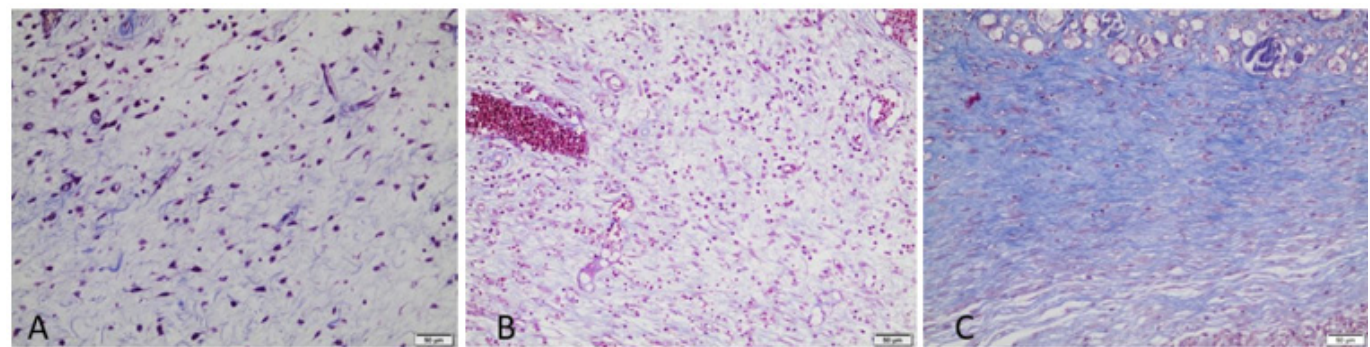


Figure 3. Evaluation of fibrosis, **A.** Mild fibrosis and a small number of stained collagen fibers observed in group 0 (Masson Trichrome X200). **B.** Minimal increase in collagen fibers at the wound base in group I (Masson Trichrome X200). **C.** Severe fibrosis in group S, characterized by a notable increase in collagen fibers stained blue (Masson Trichrome X200).

Table 3. The severity of acute inflammation, chronic inflammation, granulation, and fibrosis				
	Sham (n=7)	Isotonic (n=7)	Sevoflurane (n=7)	p*
Active inflammation				
None	0	0	0	0.443
Mild	1	3	3	
Moderate	3	3	1	
Severe	3	1	3	
Chronic Inflammation				
None	0	0	0	0.013
Mild	5	2	6	
Moderate	0	5	1	
Severe	2	0	0	
Granulation				
None	0	0	0	0.006
Mild	4	1	0	
Moderate	3	6	3	
Severe	0	0	4	
Fibrosis				
None	0	0	0	0.023
Mild	6	3	1	
Moderate	0	3	1	
Severe	1	1	5	
*Fisher Exact test was used for the comparisons of categorical variables. A value of p<0.05 was accepted as statistically significant in all the analyses.				

*Fisher Exact test was used for the comparisons of categorical variables. A value of $p < 0.05$ was accepted as statistically significant in all the analyses

While the FDA currently approves only the inhalation form of sevoflurane, there are documented case reports that highlight the benefits of topical sevoflurane use. Such cases involve venous and ischemic ulcers that exhibit resistance to standard treatments and showcase improved wound healing and reduced analgesia requirements.⁸⁻¹¹ Additionally, there are publications in the literature describing the use of topical sevoflurane in surgical wounds infected with multidrug-resistant microorganisms², vascular ulcers¹², and cancer wounds.¹ These are clinical case reports and case series with small sample sizes, but the consistent theme is that topical sevoflurane application leads to accelerated wound healing, rapid and long-lasting pain reduction, and reduced reliance on traditional analgesics. The simplicity and safety of application make it well-tolerated by patients.^{8,11,12} However, the specific mechanism of action of topically applied sevoflurane remains unclear.

To the best of our knowledge, there have been no previous studies examining the effects of topical sevoflurane on wound healing in rats. However, a previous study examining the effects

of inhaled sevoflurane on wound healing in rats reported a significantly decreased expression rate of procollagen 1 and 3, reflecting the rates of growth factor (bFGF) and collagen expression, in the group exposed to long-term (8 hours) sevoflurane compared to the group with a shorter exposure.¹³ Researchers suggested that these findings might be related to the duration of sevoflurane exposure and its systemic immunosuppressive effects.

In the current study, the effects of topical sevoflurane on active inflammation, chronic inflammation, granulation tissue, and fibrosis were assessed histopathologically. The results revealed that while there were differences among the groups in terms of active inflammation, these differences were not statistically significant. However, the severity of chronic inflammation was significantly lower in the sevoflurane group compared to the other two groups. The reduced chronic inflammation observed in the sevoflurane group supports the anti-inflammatory potential of sevoflurane. Additionally, the level of granulation tissue, marked by fibroplasia, giant cells, and increased vascularization, was significantly higher in the sevoflurane group compared to the other groups. The greater extent of fibrosis in the sevoflurane group can be interpreted as wound size reduction and accelerated wound healing. It's worth noting that the study was terminated on the 14th day due to ethical considerations and logistical challenges, preventing the evaluation of sevoflurane's effects on wound dimensions. This aspect could be explored in longer-term studies with larger sample sizes.

Prior studies have demonstrated the anti-inflammatory properties of inhaled sevoflurane.¹⁴⁻¹⁶ It has been shown to decrease the expression of pro-inflammatory cytokines such as TNF- α , IL-6, and IL-8 and reduce microglial migration caused by pro-inflammatory cytokine production. While IL-1 β is considered harmful in wound repair, it is necessary in the early stages of inflammation for wound healing. Similarly, pro-inflammatory cytokines like IL-1 β , TNF- α , and IFN- γ have been found to be essential in the early stages of wound healing, demonstrating that they are not detrimental to wound repair. Furthermore, IL-6 and IL-8 levels have been shown to decrease in patients administered intraoperative sevoflurane, indicating its suppressive effects on pro-inflammatory cytokines. IL-10, another inflammatory cytokine, has anti-inflammatory properties by suppressing the production of inflammatory cytokines and plays a crucial role in regulating pro-inflammatory cytokine expression in wounds, contributing to scar-free healing.

In contrast to some of these previous studies, the current study did not reveal statistically significant differences in the serum levels of TNF- α , IL-1 β , IL-6, and IL-10 between the groups at the examined time points. This lack of significance could be attributed to the limited sample size in the study due to ethical regulations for laboratory animals. Additionally, there is a lack of knowledge regarding the peak and decline times of cytokine expression, potentially contributing to the absence of significant results. Future studies with larger sample sizes and longer observation periods may provide more meaningful results.

The specific mechanism of action of topically applied sevoflurane remains unclear. Some case studies have indicated that topical sevoflurane could be a therapeutic option for wounds infected

with multidrug-resistant microorganisms and painful chronic venous ulcers.^{2-4,8-10} There is also a case study of a patient with ulcerative necrobiosis lipoidica diabetorum, which successfully treated the condition with topical sevoflurane and punch grafting, resulting in full epithelialization.¹

Limitations

The limitations of the current study include the small group sizes due to ethical constraints and the relatively short observation period of 14 days. To further understand the effects of topical sevoflurane, larger sample sizes and longer-term studies are needed.

This study pioneers the investigation of topical sevoflurane's effects on wound healing in a rat model, contrasting with prior research focusing on its inhaled form. Although the study is constrained by the limited subject number and duration due to ethical considerations, it opens avenues for future research to further elucidate the therapeutic potential of sevoflurane in wound management. We postulate that sevoflurane's wound healing properties may be attributed to its anti-inflammatory action, as reflected by the reduced chronic inflammation and pronounced fibroplastic activity. Such activity is crucial during the granulation phase, a pivotal stage in wound repair marked by neovascularisation and fibroplasia. The significant fibrosis observed suggests that sevoflurane may accelerate wound closure and tissue repair, a hypothesis warranting further long-term studies. Previous findings have corroborated the anti-inflammatory properties of inhaled sevoflurane,⁴⁻⁶ yet this study's lack of significant changes in plasma cytokine levels calls for additional research. Considering the limitations of subject number and study duration, extended investigations could yield more definitive insights, particularly if tissue-level cytokine expressions are examined. In summary, while the topical application of sevoflurane demonstrates promising histopathological benefits in wound healing, corroborative immunochemical evidence remains to be established. Future research should aim to extend the monitoring period and include a broader range of immunochemical parameters to substantiate the preliminary findings observed herein.

CONCLUSION

In summation, this investigation supports the premise that topical sevoflurane positively influences wound healing in a rat burn model. The histopathological data underscores a beneficial effect characterized by reduced chronic inflammation and enhanced granulation and fibrosis. These observations suggest the potential of sevoflurane as an adjunctive therapy in the management of burn injuries and wound care. However, the anticipated immunochemical support for these findings was not substantiated in plasma cytokine analysis within the study's timeframe. The absence of significant immunochemical data underscores the need for extended observation periods and a more comprehensive examination of tissue-level cytokine profiles. Such future studies could provide the necessary empirical evidence to firmly establish the therapeutic efficacy of sevoflurane for wound healing. Given the recognized anti-inflammatory effects of sevoflurane when inhaled, further research is warranted to explore its topical benefits. The pursuit of such knowledge could potentially unveil a novel therapeutic application for sevoflurane, revolutionizing wound management strategies and improving patient outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval

Approval for this investigation was obtained from the Animal Experiments Local Ethics Committee of Ankara Training and Research Hospital (Date: 26.11.2020, Decision No: 0063-646).

Informed Consent

Since this study is an animal experiment, informed consent is not required.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The study was financially supported by the Scientific Research Projects Coordination Unit of Health Sciences University Dışkapı Yıldırım Beyazıt Health Applications and Research Centre (BAP no: 78/03).

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

- Quintana-Castaneda L, Recarte-Marín L, Pérez-Jerónimo L, Conde-Montero E, de la Cueva-Dobao P. Ulcerative necrobiosis lipoidica diabetorum successfully treated with topical sevoflurane and punch grafting. *Int Wound J*. 2019;16(5):1234-1236. doi:10.1111/iwj.13179
- Rueda-Martínez JL, Gerónimo-Pardo M, Martínez-Monsalve A, Martínez-Serrano M. Topical sevoflurane and healing of a post-operative surgical site superinfected by multi-drug-resistant *Pseudomonas aeruginosa* and susceptible *Staphylococcus aureus* in an immunocompromised patient. *Surg Infect (Larchmt)*. 2014;15(6):843-846. doi:10.1089/sur.2013.079
- Imbernon-Moya A, Ortiz-de Frutos FJ, Sanjuan-Alvarez M, Portero-Sanchez I, Merinero-Palomares R, Alcazar V. Treatment of chronic venous ulcers with topical sevoflurane: a retrospective clinical study. *Br J Anaesth*. 2017;119(4):846-847. doi:10.1093/bja/aex269
- Potočnik I, Novak Janković V, Šostarič M, et. al. Antiinflammatory effect of sevoflurane in open lung surgery with one-lung ventilation. *Croat Med J*. 2014;55(6):628-637. doi:10.3325/cmj.2014.55.628
- Yu X, Zhang F, Shi J. Effect of sevoflurane treatment on microglia activation, NF-κB and MAPK activities. *Immunobiology*. 2019;224(5):638-644. doi:10.1016/j.imbio.2019.07.004
- Yu QB, Li HM, Li LL, Wang SY, Wu YB. Sevoflurane downregulates interleukin-6 and interleukin-8 levels in patients after cardiopulmonary bypass surgery: a meta-analysis. *Genet Mol Res*. 2015;14(4):19016-19027. doi:10.4238/2015.December.29.9
- Chhabra S, Chhabra N, Kaur A, Gupta N. Wound healing concepts in clinical practice of OMFS. *J Maxillofac Oral Surg*. 2017;16(4):403-423. doi:10.1007/s12663-016-0880-z
- Imbernón A, Blázquez C, Puebla A, et. al. Chronic venous ulcer treatment with topical sevoflurane. *Int Wound J*. 2016;13(5):1060-1062. doi:10.1111/iwj.12474
- Hidalgo-Doniga C, Lopez-Lopez C, Pajero Otero V, et. al. Use of topical sevoflurane in pressure ulcer treatment in a double-lung transplant patient. *J Tissue Viability*. 2021;30(1):124-127. doi:10.1016/j.jtv.2020.07.003
- Fernández-Ginés FD, Cortiñas-Sáenz M, Agudo-Ponce D, et. al. Pain reduction of topical sevoflurane vs intravenous opioids in pressure ulcers. *Int Wound J*. 2020;17(1):83-90. doi:10.1111/iwj.13235
- Su L, Zheng J, Wang Y, Zhang W, Hu D. Emerging progress on the mechanism and technology in wound repair. *Biomed Pharmacother*. 2019;117:109191. doi:10.1016/j.biopha.2019.109191
- Dámaso Fernández-Ginés F, Cortiñas-Sáenz M, Mateo-Carrasco H, et. al. Efficacy and safety of topical sevoflurane in the treatment of chronic skin ulcers. *Am J Health Syst Pharm*. 2017;74(9):176-182. doi:10.2146/ajhp151008
- Cha MS, Lee HJ, Bae JH, Yang WS, Baik SW. Effects of sevoflurane on wound healing process. *Korean J Anesthesiol*. 2009;57(1):78-83. doi:10.4097/kjae.2009.57.1.78
- Khan J, Noboru N, Young A, Thomas D. Pro and anti-inflammatory cytokine levels (TNF-α, IL-1β, IL-6 and IL-10) in rat model of neuroma. *Pathophysiology*. 2017;24(3):155-159. doi:10.1016/j.pathophys.2017.04.001
- Alzoghaibi MA, Al-Oraini AI, Al-Sagheir AI, Zubaidi AM. Temporal expression of IL-1β and IL-10 in rat skin, muscle, small bowel, and colon wounds: a correlative study. *J Basic Clin Physiol Pharmacol*. 2014;25(2):205-210. doi:10.1515/jbcpp-2013-0073
- de Waal Malefyt R, Abrams J, Bennett B, Figdor CG, de Vries JE. Interleukin 10 (IL-10) inhibits cytokine synthesis by human monocytes: an autoregulatory role of IL-10 produced by monocytes. *J Exp Med*. 1991;174(5):1209-1220. doi:10.1084/jem.174.5.1209

Comparison of interleukin-6 receptor antagonist and pulse steroid therapy in critically ill patients with COVID-19: retrospective analysis

 Filiz Koç¹,  Münire Babayiğit²,  Mustafa Alparslan Babayiğit³,  Oral Menteş⁴,
 Emine Fırat Göktaş⁵,  Necla Dereli²

¹Department of Clinical Microbiology and Infectious Diseases, Ankara Bilkent City Hospital, Ankara, Türkiye

²Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

³Public Health Specialist, Occupational Physician, Ankara, Türkiye

⁴Department of Chest Diseases and Intensive Care, Gülhane Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

⁵Department of Clinical Microbiology and Infectious Diseases, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Cite this article: Koç F, Babayiğit M, Babayiğit MA, Menteş O, Fırat Göktaş E, Dereli N. Comparison of interleukin-6 receptor antagonist and pulse steroid therapy in critically ill patients with COVID-19: retrospective analysis. *Eur J Anesthesiol Intens Care*. 2025;2(1):7-11.

Corresponding Author: Münire Babayiğit, mnroksuz@hotmail.com

Received: 15/09/2024

Accepted: 16/11/2024

Published: 03/02/2025

ABSTRACT

Aims: Severe COVID-19 is characterized by acute respiratory distress syndrome (ARDS) accompanied by hypercytokinemia. In our study, we aimed to demonstrate the efficacy of the treatments interleukin-6 (IL-6) receptor antagonists and corticosteroids used in critically ill patients with COVID-19.

Methods: COVID-patients with cytokine storm (CS) treated in the intensive care unit between March 2020 and July 2021 were included in the study. Patients with increased neutrophil/lymphocyte ratio, lactate dehydrogenase, C-reactive protein (CRP), and ferritin and patients with oxygen saturations of 90% or lower, lymphopenia and fever were also considered in CS. Patients were divided into three groups: tocilizumab group, steroid group, standard treatment group.

Results: There was no statistically significant difference between the groups in terms of age and body-mass index (BMI) averages, gender ratios and concomitant diseases. There was no difference in mortality and the need for mechanical ventilation between the groups. On the other hand, the incidence of ventilator-associated pneumonia was higher in the pulse steroid group.

Conclusion: The close and early diagnosis of hypercytokinemia increase the success of the treatment, and accelerate to discharge from intensive care units. We think that it is important to select appropriate patients and pulse steroid is more suitable for use in CS because it is cheaper and more accessible.

Keywords: COVID-19, corticosteroids, ARDS, interleukin-6, tocilizumab

INTRODUCTION

Severe COVID-19 pneumonia is characterized by acute respiratory distress syndrome (ARDS) accompanied by a hypercytokinemia, as in inflammatory cytokine release syndrome (CRS) or hemophagocytic lymphohistiocytosis (HLH)/macrophage activation (MAS) syndrome.¹⁻⁷ Published studies have shown that this disruption of interferon signaling, called cytokine storm (CS), is related to inflammatory pathology and the severity of the disease.^{8,9} Increased neutrophil/lymphocyte ratio, elevated C-reactive protein (CRP) levels, increased interleukin-6 (IL-6) levels were also associated with disease severity.¹⁰⁻¹⁴

IL-6 plays a central role in the inflammatory pathology of COVID-19, and there is a consistent association between increased cytokine levels and severe disease outcomes. Cytokine modulator therapies have been introduced to break this hyperinflammatory cycle. Reports from China and Italy, which were the most affected regions in early 2020, showed miraculous improvements with anti-IL-6 (tocilizumab) treatments. However, results from subsequent large-scale studies have shown that IL-6 modulation does not benefit every patient in the treatment of COVID-19.¹⁵ Corticosteroids, like IL-6 antagonists, have been widely used in various doses

all over the world due to their immune modulatory properties, and the studies have been announced to the scientific world. The largest of these studies is the multicenter RECOVERY study conducted in England. This study that 6 mg dexamethasone given to hospitalized COVID-19 patients for an average of 7-10 days reduced 28-day mortality. This effect was more pronounced in patients receiving mechanical ventilation or oxygen support, but this positive effect did not occur in patients who did not require oxygen support.¹⁶ After the meta-analysis of World Health Organization's (WHO) corticosteroid studies, WHO and our Ministry of Health added a low-dose steroid recommendation to the guide.¹⁷⁻¹⁹

In the next period high-dose corticosteroid treatments (pulse steroids) were started to be used in critical cases that did not respond to low-dose corticosteroid treatment, or needed intensive care due to worsening of pneumonia and rapid decrease in saturation. The first pulse steroid studies on this subject that mortality was reduced in severe COVID-19 patients.^{20,21}

With the experience gained in the treatment of critically ill patients in intensive care units, IL-6 antagonists have started to be used in combination with steroids. There are some studies supporting the use of these two medications together, as well as studies showing that the treatment has no effect. It is also recommended to be used together with the results of active ongoing study groups.²²⁻²⁶

Laboratory tests are performed to assess the severity of the disease and to observe the patient's response to treatment. Parameters such as lymphocytes, neutrophils, LDH, CRP, and ferritin, which indicate the severity of inflammation, are frequently examined. The course of these values and their ratios to each other give the physician an idea about the development of hypercytokinemia and enable him to decide on a treatment plan.

In this study, we aimed to determine the effective treatment for severe pneumonia cases accompanied by hypercytokinemia, which we treated in our intensive care unit by examining the responses of IL-6 antagonist (tocilizumab) and pulse steroid therapy.

METHODS

Ethics committee approval was obtained from the Clinical Researches Ethics Committee of the Keçiören Training and Research Hospital (Date 28.09.2021, Decision No: 2372). The study was conducted according to the Helsinki Declaration.

The patients with CS were divided into three groups those who received an IL-6 receptor antagonist (n=14, tocilizumab 800 mg/day), pulsed corticosteroids (n=30, methylprednisolon 250 mg/day), control group (n=37) who were followed up with standard treatment without these treatments.

Blood samples were taken from the patients on the day of admission to the intensive care unit, during the hypercytokinemia period and afterwards. The results of the hemogram and biochemical tests at these times were analyzed.

Patients with increased neutrophil/lymphocyte ratio, high LDH, CRP, and ferritin (>700 ng/ml) levels, and those whose values continued to increase in consecutive measurements and

patients with oxygen saturations of 90% or lower, lymphopenia and persistent fever (>38 C°) were also considered to be in CS. Patients' age, gender, weight, nutritional scores (nutric score), comorbidities, treatments, length of stay intensive care unit, acute physiology and chronic health evaluation (APACHE) II scores, lymphocytes, neutrophils, LDH, CRP, D-Dimer, ferritin levels, arterial blood gas analysis results, secondary infections, and mortality rates were recorded and analyzed.

Statistical Analysis

Continuous variables were expressed as mean±standard deviation, categorical data as numbers and percentages. In the intergroup analysis of continuous variables, normality analyzes were performed with the Kolmogorov-Smirnov Goodness of Fit test. The Oneway ANOVA test (Post hoc: Bonferroni) was used for the analysis of data within normal distribution, and the Kruskal-Wallis test (Mann-Whitney U test with Bonferroni correction) was used for the analysis of data out of normal distribution. Comparisons of categorical data were made with the Chi-square test. Analyzes were performed with IBM SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). Statistical significance level was considered as $p < 0.05$.

RESULTS

There was no statistically significant difference between the groups in terms of age and body-mass index (BMI) averages and gender ratios ($p > 0.05$). The rates of patients with a nutric score of three or more were 57.1% in the tocilizumab group, 93.3% in the pulse steroid group, and 47.2% in the control group ($p = 0.002$). There was no significant difference between the groups in terms of comorbidities like chronic obstructive pulmonary disease, asthma, hypertension, diabetes mellitus, coronary artery diseases, cerebrovascular disease, chronic kidney failure, and immunosuppressive use rates ($p > 0.05$) (Table 1).

It was determined that length of stay in hospital, the intensive care unit and the ward (pre ICU), the partial oxygen pressure/oxygen fraction (P/F) ratios at ICU admission, and initial lactate values were statistically significantly higher in the tocilizumab group compared to the steroid group and the control group ($p < 0.05$). The duration of mechanical ventilation was found to be statistically significantly higher in the tocilizumab group than in the steroid group ($p: 0.019$) (Table 2).

While there was no difference in the rate of nasocomial infection between the groups, the rate of ventilator-associated pneumonia was found to be highest in group receiving steroid treatment in terms of focus of infection ($p: 0.016$). The most frequently detected bacteria in all groups was *Acinetobacter baumannii* (71.4-91.7%), followed by *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (Table 2).

In the tocilizumab group, the lymphocyte values after CS were found to be statistically significantly lower than the control group ($p = 0.001$), and the ferritin values after CS were found to be significantly higher ($p = 0.001$). Lymphocyte level during and after CS in the steroid group was found to be lower than the other two groups. Ferritin and LDH values after CS were found to be statistically significantly lower in the group receiving standard treatment compared to the control group ($p = 0.001$, $p < 0.001$, respectively) (Table 3).

Table 1. Comparison of the groups in terms of some socio-demographic and clinical characteristics

	Tocilizumab group (n=14)	Steroid group (n=30)	Standard treatment group (n=37)	p value
Age (mean±SD)	59.14±13.43	65.37±15.59	67.46±14.99	0.215*
BMI (kg/m ²) (mean±SD)	30.48±5.20	30.90±5.89	30.21±6.75	0.904*
Gender (n,%)				
Female	4 (28.6%)	10 (33.3%)	17 (45.9%)	0.409**
Male	10 (71.4%)	20 (66.7%)	20 (54.1%)	
Nutric score (n, %)				
0				0.002**
1	6 (42.9%)	1 (3.3%)	12 (33.3%)	
2	0 (0.0%)	1 (3.3%)	7 (19.4%)	
3	5 (35.7%)	16 (53.3%)	12 (33.3%)	
4	3 (21.4%)	12 (40.0%)	5 (13.9%)	
COPD (n, %)	3 (21.4%)	5 (16.7%)	3 (8.1%)	0.382**
Asthma (n, %)	2 (14.3%)	0 (0.0%)	4 (10.8%)	0.136**
HT (n, %)	4(28.6%)	17 (56.7%)	17 (45.9%)	0.404**
DM (n, %)	5 (35.7%)	16 (53.3%)	12 (32.4%)	0.144**
CAD (n, %)	1 (7.1%)	6 (20.0%)	7 (18.9%)	0.540**
CVD (n, %)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0.089**
CKD (n, %)	0 (0.0%)	3 (10.0%)	1 (2.7%)	0.252**
Favipiravir (n, %)	12 (85.7%)	29 (96.7%)	31 (83.8%)	0.228**

* Oneway ANOVA test, ** Chi-square test, SD: Standard deviation, BMI: Body-mass index, COPD: Chronic obstructive pulmonary disease, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary arterial disease, CVD: Cerebrovascular disease, CKD: Chronic kidney disease

Table 2. Comparison of the groups in terms of clinical parameters related to hospitalization and intensive care unit stay

	Tocilizumab group (n=14)	Steroid group (n=30)	Standard treatment group (n=37)	p value
LOS in hospital (day) (mean±SD)	30.48±5.20 ^a	17.57±7.82 ^a	25.38±17.07	0.003*
LOS in the ICU (day) (mean±SD)	23.64±16.27	13.17±7.78	19.16±17.49	0.063*
APACHE II score (mean±SD)	14.78±5.69	17.10±5.22	19.75±10.47	0.125*
LOS in the ward (day) [median (min-max)]	4.5 (0-12) ^b	1 (0-7) ^b	1 (0-9)	0.016**
P/F ratio [median (min-max)]	143.5(63-295) ^b	74.5 (48-117) ^b	77 (42-250) ^b	0.002**
Initial lactate level [median (min-max)]	0.92(0.29-0.18) ^b	1.53(0.80-6.97) ^b	1.19 (0.08-11.7)	0.004**
MV (n, %)	8 (57.1%)	16 (53.3%)	22 (59.5%)	0,881***
MV support (day) [median (min-max)]	22 (17-59)	11 (1-33)	15.5 (1-84)	0.019**
Secondary infection (n, %)	4 (28.5%)	9 (30.0%)	12 (32.4)	0.957***
Infection type (n, %)				
VAP	0 (0.0%)	8 (100.0%)	6 (50.0%)	0.016***
UTI	1 (25.0%)	0 (0.0%)	0 (0.0%)	
Central catheter	1 (25.0%)	0 (0.0%)	3 (25.0%)	
Blood circulation	1 (25.0%)	0 (0.0%)	3 (25.0%)	
Surgical field	1 (%25.0)	0 (0.0%)	0 (0.0%)	
Microorganism (n, %)				
<i>Klebsiella</i>	0 (0.0%)	1 (14.3%)	1 (8.3%)	0.527***
<i>Pseudomonas</i>	1 (25.0%)	1 (14.3%)	0 (0.0%)	
<i>Acinetobacter</i>	3 (75.0%)	5 (71.4%)	11 (91.7%)	
Mortality (n, %)	4 (28.6%)	16 (53.3%)	15 (40.5%)	0.275***

* Oneway ANOVA test (aPostoc: Bonferroni corrected), ** Kruskal Wallis test (a,b Mann Whitney U test with Bonferroni correction), *** Chi-square test, LOS in hospital: Length of stay in hospital, LOS in ICU: Length of stay in the intensive care unit, LOS in ward: Length of stay in the ward (pre ICU), APACHE II score: Acute physiology and chronic health evaluation II score, P/F ratio: PaO₂/FiO₂ at admission to ICU, MV: Mechanical ventilation, VAP: Ventricle-associated pneumonia, UTI: Urinary tract infections, SD: Standard deviation, Min-max: Minimum-maximum

Table 3. Comparison of the groups in terms of some inflammatory markers

	Tocilizumab group (n=14)	Steroid group (n=30)	Standard treatment group (n=37)	p value
CRP*				
CS period	310 (42-469)	255 (95-384)	272 (68-491)	0.407**
Post CS	13.5 (1.5-218)	15 (2.2-124)	16 (0.12-223)	0.741**
Lymphocyte *				
CS period	375 (100-740)	330 (30-700) ^b	470(180-1770) ^b	0.008**
Post CS	1370 (290-2330) ^a	1070 (310-11800) ^b	2410(660-5200) ^{a,b}	<0.001**
Ferritin*				
CS period	1301.5(592-11391)	1242 (84-12286)	931 (178-4687)	0.546**
Post CS	429 (77-1470) ^a	445.5 (35-1296) ^b	225.5 (26-734) ^{a,b}	0.001**
D-dimer*				
CS period	4265 (820-15440)	3670 (1220-35200)	4340(780-44980)	0.719**
Post CS	735 (220-2300)	625 (260-2120)	540 (170-2150)	0.090**
LDH*				
CS period	557.5(348-3315)	676 (309-2363)	621 (233-2851)	0.198**
Post CS	288 (172-669)	309 (161-806) ^b	228 (133-543) ^b	<0.001**

* Values are given as median (minimum-maximum) initial value measured during hypercytokinemia,**Kruskal Wallis test (a,b Mann Whitney U test with Bonferroni correction), CS: Cytokine storm

DISCUSSION

In this study we examined COVID-19 patients who developed CS and were treated with pulse steroids or tocilizumab. The length of stay in hospital before intensive care unit, the length of stay in the intensive care unit, the P/F ratios and LDH levels of the patients who received tocilizumab were found to be high and the duration of mechanical ventilation was longer in the tocilizumab group.

In the meta-analysis of Tleyjeh et al.¹⁵ investigating the efficacy and safety of tocilizumab in COVID-19 patients, a decrease was found in the length of hospital stay and mechanical ventilation, but no decrease in mortality in the short term. In addition, there was no increase in side effects and nosocomial infections, and these effects were thought to be important for reducing mortality. In our study, the length of hospital stay, intensive care unit stay and total hospital stay was longer in the tocilizumab group. However, it was the group with the lowest secondary infection rate. This might be related to the efficacy of infection control, despite long hospital stays in our hospital's intensive care unit and services.

Prior to the introduction of low-dose steroids into treatment guidelines, the RECOVERY preliminary report noted that various high doses were widely used and promising in the treatment of COVID-19 hypercytokinemia.¹⁶ After RECOVERY, several studies have reported that pulse steroid reduces mortality in patients with hypercytokinemia who do not respond to low-dose steroids.^{20,21} Although there was no difference in the rate of nosocomial infections in this patient group, the prevalence of ventilator associated pneumonia (VAP) in infections suggests that it prevents a decrease in mortality.²⁷ We think that these infections are due to the predisposition of steroids to serious infections.

A meta-analysis of 73 studies by Cano et al.²⁸ including 21350 cases stated that low-dose steroid administered in these patient groups reduced mortality, and that there was no difference in mortality and side effects between high-dose and low-dose. In our study, although there was no difference in the rate of nosocomial infections between our groups, there was a significant difference in the focus of nosocomial infections. VAP was more common in patients receiving pulse steroids. Since the target organ of the disease is the lung, VAP is primarily the expected nosocomial infection. It is thought that high VAP rates prevent a decrease in mortality rates. No difference was found between the groups in the agents in our study. The same agents were reported in similar patient groups.²⁹

Limitations

Analyzing a small patient group from a single center can be considered as a limitation of our study. However, it is important for each center to conduct and share treatment analysis results, especially for specific diseases, in terms of creating a resource for meta-analyses. For this purpose, we believe that the results of our study will contribute to the literature.

CONCLUSION

With the use of low-dose corticosteroids in the treatment, hypercytopenia was easily controlled in many patients, and the use of IL-6 antagonists and the need for intensive care were significantly reduced. Early treatment is also effective

in the success of the treatment in the patient group who need intensive care due to their serious clinics and accelerates the process of discharge from these units. Although both treatment models have their shortcomings, we think that appropriate patient selection is important and because it is cheaper and more accessible, pulse steroids can be preferred in suitable patients in CS.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethics committee approval was obtained from the Clinical Researches Ethics Committee of the Keçiören Training and Research Hospital (Date 28.09.2021, Decision No: 2372).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. World Health Organization. 2021. WHO coronavirus (COVID-19) dashboard. (Accessed November 2021). <https://covid19.who.int/>.
2. Fajgenbaum DC, June CH. Cytokine storm. *N Engl J Med*. 2020;383(23):2255-2273. doi:10.1056/NEJMra2026131
3. McGonagle D, Sharif K, O'Regan A, Bridgewood C. The role of cytokines including interleukin-6 in COVID-19 induced pneumonia and macrophage activation syndrome-like disease. *Autoimmun Rev*. 2020;19(6):102537. doi:10.1016/j.autrev.2020.102537
4. Opoka-Winiarska V, Grywalska E, Roliński J. Could hemophagocytic lymphohistiocytosis be the core issue of severe COVID-19 cases? *BMC Med*. 2020;18(1):214. doi:10.1186/s12916-020-01682-y
5. Pedersen SE, Ho YC. SARS-CoV-2: a storm is raging. *J Clin Invest*. 2020;130(5):2202-2205. doi:10.1172/JCI137647
6. Xu X, Han M, Li T, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci USA*. 2020;117(20):10970-10975. doi:10.1073/pnas.2005615117
7. Zhang W, Zhao Y, Zhang F, et al. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): the perspectives of clinical immunologists from China. *Clinical Immunology*. 2020;214:108393. doi:10.1016/j.clim.2020.108393
8. Bastard P, Rosen LB, Zhang Q, et al. Autoantibodies against type I IFNs in patients with life-threatening COVID-19. *Science*. 2020;370(6515):eabd4585. doi:10.1126/science.abd4585
9. Zhang Q, Bastard P, Liu Z, et al. Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. *Science*. 2020;370(6515):eabd4570. doi:10.1126/science.abd4570
10. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect*. 2020;81(1):e6-e12. doi:10.1016/j.jinf.2020.04.002
11. ang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84:106504. doi:10.1016/j.intimp.2020.106504

12. Boyiadzis M, Bishop MR, Abonour R, et al. The society for immunotherapy of cancer consensus statement on immunotherapy for the treatment of hematologic malignancies: multiple myeloma, lymphoma, and acute leukemia. *J Immunother Cancer*. 2016;4(1):90. doi:10.1186/s40425-016-0188-z
13. Herold T, Jurinovic V, Arnreich C, et al. Elevated levels of IL-6 and CRP predict the need for mechanical ventilation in COVID-19. *J Allergy Clin Immunol*. 2020;146(1):128-136.e4. doi:10.1016/j.jaci.2020.05.008
14. Laguna-Goya R, Utrero-Rico A, Talayero P, et al. IL-6-based mortality risk model for hospitalized patients with COVID-19. *J Allergy Clin Immunol*. 2020;146(4):799-807.e9. doi:10.1016/j.jaci.2020.07.009
15. Tleyjeh IM, Kashour Z, Damlaj M, et al. Efficacy and safety of tocilizumab in COVID-19 patients: a living systematic review and meta-analysis. *Clin Microbiol Infect*. 2021;27(2):215-227. doi:10.1016/j.cmi.2020.10.036
16. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med*. 2021;384(8):693-704. doi:10.1056/NEJMoa2021436
17. WHO rapid evidence appraisal for COVID-19 therapies (REACT) working group, Sterne JAC, Murthy S, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA*. 2020;324(13):1330-1341. doi:10.1001/jama.2020.17023
18. World Health Organization. Corticosteroids for COVID-19: living guidance, 2 September 2020. World Health Organization.
19. Turkish Ministry of Health COVID-19 guideline: anticytokin antiinflammatory therapies coagulopathy treatment. 2 November 2020. Ankara.
20. Edalatifard M, Akhtari M, Salehi M, et al. Intravenous methylprednisolone pulse as a treatment for hospitalised severe COVID-19 patients: results from a randomised controlled clinical trial. *Eur Respir J*. 2020;56(6):2002808. doi:10.1183/13993003.02808-2020
21. Cusacovich I, Aparisi Á, Marcos M, et al. Corticosteroid pulses for hospitalized patients with COVID-19: effects on mortality. *Mediators Inflamm*. 2021;2021:6637227. doi:10.1155/2021/6637227.
22. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. <https://covid19treatmentguidelines.nih.gov/> (Accessed on May 27, 2022).
23. Infectious diseases society of American Guidelines on the treatment and management of patients with COVID-19 <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/> (Accessed on February 21, 2022).
24. Aziz M, Haghbin H, Abu Sitta E, et al. Efficacy of tocilizumab in COVID-19: a systematic review and meta-analysis. *J Med Virol*. 2021;93(3):1620-1630. doi:10.1002/jmv.26509
25. Malgie J, Schoones JW, Pijls B.G. Decreased mortality in COVID-19 patients treated with Tocilizumab: a rapid systematic review and meta-analysis of observational studies. *Clin Infect Dis*. 2021;72(11):e742-e749. doi:10.1093/cid/ciaa1445
26. Gupta S, Wang W, Hayek SS, et al. Association between early treatment with tocilizumab and mortality among critically ill patients with COVID-19. *JAMA Intern Med*. 2021;181(1):41-51. doi:10.1001/jamainternmed.2020.6252
27. Stuck AE, Minder CE, Frey FJ. Risk of infectious complications in patients taking glucocorticosteroids. *Rev Infect Dis*. 1989;11(6):954-963. doi:10.1093/clinids/11.6.954
28. Cano EJ, Fonseca Fuentes X, Corsini Campioli C, et al. Impact of Corticosteroids in coronavirus disease 2019 outcomes: systematic review and meta-analysis. *Chest*. 2021;159(3):1019-1040. doi:10.1016/j.chest.2020.10.054
29. Yılmaz B, Ergut Sezer B, Günkaya M, Onar LÇ, Sivri F. Yoğun bakımda COVID-19 pnömonisi hastalarında tosilizumab kullanımı: olgu serisi. *J Turk Soc Intens Care*. 2020;18:61-66. doi:10.4274/tybd.galenos.2020.19483

Assessment of YouTube videos on ultrasound-guided lower extremity peripheral nerve blocks

 **Esra Göger**

Department of Anesthesiology and Reanimation, Konya City Hospital, Konya, Türkiye

Cite this article: Göger E. Assessment of YouTube videos on ultrasound-guided lower extremity peripheral nerve blocks. *Eur J Anesthesiol Intens Care.* 2025;2(1):12-17.**Corresponding Author:** Esra Göger, dr.esragoger@gmail.com**Received:** 06/11/2024**Accepted:** 29/11/2024**Published:** 03/02/2025

ABSTRACT

Aims: Numerous YouTube videos on lower extremity nerve blocks, frequently utilized for analgesia in anesthesia practice, are available to the public. To prevent the spread of incorrect or incomplete information and reduce information pollution, it is essential to review these videos critically. Accordingly, this study assessed the educational content and preparation quality of videos on YouTube about lower extremity nerve block.

Methods: Two structured surveys assessed ten different types of lower extremity nerve block educational videos on YouTube. Each survey comprises 14 questions, each scored on a scale from 0 to 5. This results in a total possible score between 0 and 70 for each video per survey.

Results: A statistically significant and strong correlation was observed between the video preparation quality score and the video educational quality score ($p < 0.001$). Additionally, there was a statistically significant positive association between the number of video likes and both the video preparation quality score and the video educational quality score ($p < 0.05$ for each).

Conclusion: While YouTube provides a range of medical training videos, concerns persist regarding the reliability of this content. Consequently, obtaining medical information from reputable sources such as peer-reviewed academic journals or publications issued by official medical organizations offers a more accurate and dependable foundation for research.

Keywords: Analgesia, lower extremity nerve blocks, regional anesthesia, YouTube videos

INTRODUCTION

Founded in 2005, YouTube has become one of the world's largest video platforms, hosting a vast range of content and millions of videos. Users can access information across diverse fields, including educational content, entertainment, news, and the arts. Platforms like YouTube allow individuals to acquire new skills and gain insights into various topics by offering information from multiple perspectives.¹ YouTube can be a valuable resource for quick and easy access to medical information, assisting in health-related topics. While the widespread use of these platforms facilitates access to accurate and reliable information, it may also make finding correct information challenging, potentially leading to misinformation, especially in health matters. Accessing accurate and trustworthy information in healthcare is essential. Medical videos on YouTube are an indispensable tool for healthcare professionals and medical students.

Moreover, this content can make a significant contribution to learning. However, there are important considerations for viewers when watching these videos, such as verifying sources, prioritizing credible information, focusing on content grounded in scientific evidence, and seeking expert opinions.²⁻⁶ Some health videos may be created by individuals who still need to gain experience in their fields of expertise. In such cases, doubts may arise regarding the content's accuracy, reliability, and scientific foundation. Additionally, some videos may contain misleading or incorrect information, potentially misleading viewers.^{7,8} There is a substantial body of literature evaluating videos on interfascial plane nerve blocks and upper extremity peripheral nerve blocks available on platforms like YouTube.⁸⁻¹² Some studies have assessed the educational content quality and production quality of these videos.^{8,9,12,13} Although numerous studies have evaluated regional anesthesia

videos on YouTube, more literature is needed regarding the assessment of videos related to lower extremity nerve blocks on this platform. Anesthesiologists and anesthesia residents commonly perform lower extremity nerve blocks to reduce postoperative pain and for anesthetic purposes. This study aims to evaluate the quality of educational content and the production of videos on ten different types of lower extremity nerve blocks available on YouTube.

METHODS

Ethical committee approval was not required because this study did not involve human or animal subjects. Searching for and recording video URLs on YouTube was completed in a single session on 10/31/2024. The video search was conducted using the YouTube search engine with the following terms: “lumbar plexus block ultrasound, suprainguinal fascia iliaca block (SIFIB) ultrasound, pericapsular nerve group (PENG) block ultrasound, femoral block ultrasound, lateral femoral cutaneous nerve (LFCN) block ultrasound, adductor canal block ultrasound, obturator nerve block ultrasound, interspace between the popliteal artery and capsule of the posterior knee (IPACK) block ultrasound, sciatic nerve block ultrasound, popliteal nerve block ultrasound.” The videos were filtered and ranked by view count, with the top 5 most-watched videos for each block recorded, as view counts dropped significantly after the first five videos. Five anesthesiologists with at least 8 years of clinical experience in lower extremity peripheral nerve blocks reviewed and evaluated the videos. Two separate surveys were used to assess the YouTube videos: survey 1 evaluated the educational content, and survey 2 evaluated the quality of the videos.

Inclusion Criteria

English-language, ultrasound-guided, and videos on lower extremity peripheral nerve blocks.

Exclusion Criteria

Non-English videos, videos without ultrasound imaging, irrelevant videos, silent videos, duplicate videos, videos shorter than 1 minute and longer than 20 minutes (as extreme video lengths may compromise the objectivity of the evaluation).

Survey 1 consists of 14 questions related to the quality of the educational content of the videos. This survey form was developed based on previous studies (Table 1).^{11,13,14}

Table 1. Video educational content quality evaluation

Survey 1

1. Are the clinical indications for the block clearly explained?
2. Are anatomical landmarks clearly explained or marked?
3. Has the block anatomy been clearly explained?
4. Has the suspected mechanism of action been clearly explained?
5. Has technical information regarding probe selection and frequency of the ultrasound device been explained?
6. Has ultrasound anatomy been clearly demonstrated and explained?
7. Were the recorded sono-anatomical images and anatomical structures in the recording clear and easy to perceive?
8. Was the ultrasound image of the needle visible and easy to follow?
9. Are instructions for depth, alignment, and direction of needle movements clearly explained?
10. Has information regarding the spread of local anesthetic been explained?
11. Is information about in-plane or out-of-plane techniques given in the video?
12. Has the sterile technique been clearly explained or emphasized?
13. Has the information regarding the local anesthetic agent been explained clearly?
14. Have the possible complications associated with this block technique been explained?

Survey 2 consists of 14 questions assessing the production quality of the videos (Table 2). It was developed following guidelines prepared by the National Career Development Association (NCDA).¹⁵

Table 2. Video preparation quality assessment

Survey 2

1. Is the purpose of the video clearly stated and explained in the first quarter of the video?
2. Was the title or name of the video appropriate to the purpose of the video?
3. Were the design and content of the video suitable for the intended educational purpose?
4. Have the skills and technique of the procedure been explained using a standard, comparable, “step-by-step” method?
5. Was the information provided in the video useful for viewers to develop/improve their skill base?
6. Was the content of the video appropriate for the health and safety of both the patient and the practitioner?
7. Was the quality of the picture acceptable in terms of colors and clarity?
8. Was the quality of the video audio acceptable? (No sounds should be scored as zero)
9. Was the length of the video balanced with the content of the video?
10. Is information regarding production or release date, producers and references clearly explained?
11. Are the objectives, learning tasks, and terminology clearly stated in the video to enable viewers to perform these tasks?
12. Does the video contain additional aids such as stop-and-discuss points, scenarios, and/or a summary of the procedure?
13. Has information been provided about a way to evaluate the effectiveness and repeatability of the video?
14. Did the content of the video encourage viewers to move from passive spectators to active practitioners in the implementation of the practice?

The anesthesiologists evaluating the videos scored each question on a scale from 0 to 5 (0=very bad, 1=bad, 2=it will do, 3=good, 4=very good, 5=perfect). Each video received a total score between 0 and 70, based on the questions in survey 1 and survey 2 (0-14: very bad, 15-28: bad, 29-42: it will do, 43-56: good, 57-70: very good).

The Following Data were Recorded for the Videos

We recorded the relevant URLs of the videos, video duration, number of days the videos had been accessible, view count, source of the videos (whether academic or not), the total number of likes, and the scores given by experts on survey 1, and survey 2.

Statistical Analysis

The data obtained in the study were analyzed using the IBM Statistical Package for Social Sciences (IBM-SPSS Inc., Chicago, IL, USA) version 26.0. The normality of data distribution was assessed with the Shapiro-Wilk test. Continuous variables were expressed as median (25-75 percentile) based on their distribution, and categorical variables were presented as frequency and percentage. Spearman's rho correlation test was applied to the correlation analyses of continuous variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The words “SIFIB ultrasound, PENG block ultrasound, femoral block ultrasound, LFCN block ultrasound, adductor canal block ultrasound, obturator nerve block ultrasound, IPACK block ultrasound, sciatic nerve block ultrasound, popliteal nerve block ultrasound” were posted on YouTube. The first five most watched videos for each block (50 videos) were evaluated (Table 3). When video characteristics are evaluated, “number

of video views” is 81027 (33339-143113) (median (25-75 percentile), “number of video likes” is 440 (205-740) (median (25-75 percentile), and “video duration (seconds)” is 315 (247-452) (median (25-75 percentile). The video educational quality score was 11 videos (22%), “bad,” 37 videos (74%), “it will do,” and 2 videos (4%) “good,” the median (25-75 percentile). The video educational quality score was 29 (19-36). The video preparation quality score was 11 videos (22%) with “bad,” 37 videos (74%) with “It will do,” and 2 videos (4%) with “good” median (25-75 percentile). The video preparation quality score was 35 (31-40) (Table 3).

Table 3. Video characteristics, and quality score values

Video characteristic feature	n (%) median (25-75 th percentile)
Video views	81027 (33339-143113)
Number of video likes	440 (205-740)
Video duration (seconds)	315 (247-452)
Video educational quality score	29 (19-36)
Video educational quality score classification	Very bad 2 (4%)
	Bad 23 (46%)
	It will do 23 (46%)
	Good 2 (4%)
Video preparation quality score	35 (31-40)
Video preparation quality score classification	Bad 11 (22%)
	It will do 37 (74%)
	Good 2 (4%)
Group	LPB 5 (10%)
	SIFIB 5 (10%)
	PENG 5 (10%)
	FNB 5 (10%)
	LFCN 5 (10%)
	ACB 5 (10%)
	ONB 5 (10%)
	IPACK 5 (10%)
	SNB 5 (10%)
	PNB 5 (10%)

LPB: Lumbar plexus block, SIFIB: Suprainguinal fascia iliaca block, PENG: Pericapsular nerve group block, FNB: Femoral nerve block, LFCN: Lateral femoral cutaneous nerve block, ACB: Adductor canal block, ONB: Obturator nerve block, IPACK: Interspace between the popliteal artery and capsule of the posterior knee block, SNB: Sciatic nerve block, PNB: Popliteal nerve block

The 14 parameters and evaluation scores examined for the video educational quality score were shown separately. The three parameters most marked for the video, with “very bad” as the evaluation score, were “Was the sterile technique clearly explained or emphasized?” There were 31 videos (62%) for the option, 28 videos (56%) for the option “Was the information regarding the local anesthetic agent explained clearly?” and 28 videos (56%) for the option “Have possible complications related to this block technique been explained?”. The two parameters most marked for the video with “very good” as an evaluation score were “Was the block anatomy clearly explained?” 20 videos (40%) for the option and “Are anatomical landmarks clearly explained or marked?” For the option, there were 16 videos (32%) (Table 4).

The 14 parameters and evaluation scores examined for the video preparation quality score were shown separately. The one parameter most marked for the video was “very bad” as an evaluation score, with 25 videos (50%) for the option “Was information provided about a way to evaluate the effectiveness and repeatability of the video?”. As an evaluation score, “good, very good, and perfect” are the parameters marked for most videos, and “was the title or name of the video appropriate to the purpose of the video?” (23 videos (46%), 20 videos (40%), and 1 video (2%), respectively) (Table 5).

In examining the relationship between video educational quality score, video preparation quality score, and video

Table 4. Video educational quality questions

Question	Degree	n (%)
Are the clinical indications for the block clearly explained?	Very bad	13 (26%)
	Bad	7 (14%)
	It will do	11 (22%)
	Good	14 (14%)
	Very good	5 (10%)
	Perfect	0 (0%)
Are anatomical landmarks clearly explained or marked?	Very bad	0 (0%)
	Bad	1 (2%)
	It will do	6 (12%)
	Good	27 (54%)
	Very good	16 (32%)
	Perfect	0 (0%)
Was the block anatomy clearly explained?	Very bad	0 (0%)
	Bad	4 (8%)
	It will do	6 (12%)
	Good	20 (40%)
	Very good	20 (40%)
	Perfect	0 (0%)
Has the suspected mechanism of action been clearly explained?	Very bad	13 (26%)
	Bad	18 (36%)
	It will do	14 (28%)
	Good	5 (10%)
	Very good	0 (0%)
	Perfect	0 (0%)
Has technical information regarding probe selection and frequency of the ultrasound device been explained?	Very bad	10 (20%)
	Bad	9 (18%)
	It will do	9 (18%)
	Good	14 (28%)
	Very good	8 (16%)
	Perfect	0 (0%)
Has ultrasound anatomy been clearly demonstrated and explained?	Very bad	0 (0%)
	Bad	3 (6%)
	It will do	11 (22%)
	Good	20 (40%)
	Very good	16 (32%)
	Perfect	0 (0%)
Were the recorded sono-anatomical images and anatomical structures in the recording clear and easy to perceive?	Very bad	2 (4%)
	Bad	4 (8%)
	It will do	10 (20%)
	Good	21 (42%)
	Very good	13 (26%)
	Perfect	0 (0%)
Was the ultrasound image of the needle visible and easy to follow?	Very bad	8 (16%)
	Bad	4 (8%)
	It will do	11 (22%)
	Good	15 (30%)
	Very good	12 (24%)
	Perfect	0 (0%)
Are instructions for depth, alignment, and direction of needle movements clearly explained?	Very bad	14 (28%)
	Bad	11 (22%)
	It will do	11 (22%)
	Good	12 (24%)
	Very good	2 (4%)
	Perfect	0 (0%)
Has information regarding local anesthetic dissemination been explained?	Very bad	13 (26%)
	Bad	4 (8%)
	It will do	18 (36%)
	Good	11 (22%)
	Very good	4 (8%)
	Perfect	0 (0%)
Was information given about the in-plane or out-of-plane technique in the video?	Very bad	5 (10%)
	Bad	12 (24%)
	It will do	16 (32%)
	Good	15 (30%)
	Very good	2 (4%)
	Perfect	0 (0%)
Has sterile technique been clearly explained or emphasized?	Very bad	31 (62%)
	Bad	3 (6%)
	It will do	11 (22%)
	Good	4 (8%)
	Very good	1 (2%)
	Perfect	0 (0%)
Was the information regarding the local anesthetic agent explained clearly?	Very bad	28 (56%)
	Bad	2 (4%)
	It will do	7 (14%)
	Good	11 (22%)
	Very good	2 (4%)
	Perfect	0 (0%)
Have possible complications related to this block technique been explained?	Very bad	28 (56%)
	Bad	3 (6%)
	It will do	8 (16%)
	Good	10 (20%)
	Very good	1 (2%)
	Perfect	0 (0%)

Table 5. Video preparation quality questions

Question	Degree	n (%)
Is the purpose of the video clearly stated and explained in the first quarter of the video?	Very bad	6 (12%)
	Bad	6 (12%)
	It will do	15 (30%)
	Good	17 (34%)
	Very good	6 (12%)
Was the title or name of the video appropriate to the purpose of the video?	Perfect	0 (0%)
	Very bad	0 (0%)
	Bad	2 (4%)
	It will do	4 (8%)
	Good	23 (46%)
Were the design and content of the video suitable for the intended educational purpose?	Very good	20 (40%)
	Perfect	1 (2%)
	Very bad	0 (0%)
	Bad	0 (0%)
	It will do	12 (24%)
Have the skills and technique of the procedure been explained using a standard, comparable, "step-by-step" method?	Good	26 (52%)
	Very good	12 (24%)
	Perfect	0 (0%)
	Very bad	1 (2%)
	Bad	5 (10%)
Was the information provided in the video useful for viewers to develop/improve their skill base?	It will do	20 (40%)
	Good	18 (36%)
	Very good	6 (12%)
	Perfect	0 (0%)
	Very bad	0 (0%)
Was the content of the video appropriate for the health and safety of both the patient and the practitioner?	Bad	0 (0%)
	It will do	9 (18%)
	Good	24 (48%)
	Very good	17 (34%)
	Perfect	0 (0%)
Was the quality of the picture acceptable in terms of colors and clarity?	Very bad	3 (6%)
	Bad	8 (16%)
	It will do	14 (28%)
	Good	15 (30%)
	Very good	10 (20%)
Was the quality of the video audio acceptable? (No sounds should be scored as zero)	Perfect	0 (0%)
	Very bad	0 (0%)
	Bad	5 (10%)
	It will do	9 (18%)
	Good	26 (52%)
Was the length of the video balanced with the content of the video?	Very good	10 (20%)
	Perfect	0 (0%)
	Very bad	6 (12%)
	Bad	11 (22%)
	It will do	22 (44%)
Is information about the production or release date, producers and references clearly explained?	Good	10 (20%)
	Very good	1 (2%)
	Perfect	0 (0%)
	Very bad	2 (4%)
	Bad	8 (16%)
Are the objectives, learning tasks, and terminology clearly stated in the video to enable viewers to accomplish these tasks?	It will do	26 (52%)
	Good	14 (28%)
	Very good	0 (0%)
	Perfect	0 (0%)
	Very bad	9 (18%)
Does the video include additional aids such as stop-and-discuss points, scenarios, and/or summary of the procedure?	Bad	7 (14%)
	It will do	11 (22%)
	Good	21 (42%)
	Very good	2 (4%)
	Perfect	0 (0%)
Was information provided about a way to evaluate the effectiveness and repeatability of the video?	Very bad	25 (50%)
	Bad	7 (14%)
	It will do	17 (34%)
	Good	0 (0%)
	Very good	1 (2%)
Did the content of the video encourage viewers to shift from passive spectators to active practitioners in the implementation of the practice? technical?	Perfect	0 (0%)
	Very bad	0 (0%)
	Bad	1 (2%)
	It will do	5 (10%)
	Good	25 (50%)
	Very good	19 (38%)
	Perfect	0 (0%)

characteristics, a statistically significant positive correlation was found between the video educational quality score and the number of video likes. Regarding the relationship between video preparation quality score and video characteristics, there was a statistically significant positive correlation between the number of video likes and video duration. A strong positive correlation was also observed between video education and preparation quality (Table 6).

Table 6. Relationship between video evaluation scores and video characteristics

Characteristic property	Video educational quality score		Video preparation quality score	
	R-value	p value	R-value	p value
Video views	0.13	0.39	0.084	0.56
Number of video likes	0.395	<0.05	0.3	<0.05
Video duration (seconds)	0.255	0.074	0.278	0.05
Video educational quality score			0.804	<0.001
Video preparation quality score	0.804	<0.001		

DISCUSSION

In this study, in examining the relationship between video educational quality score, video preparation quality score, and video characteristics, a statistically significant positive correlation was found between the video educational quality score and the number of video likes. Regarding the relationship between video preparation quality score and video characteristics, there was a statistically significant positive correlation between the number of video likes and video duration. A strong positive correlation was also observed between video education and preparation quality.

Visual information is as important as theoretical knowledge in lower extremity nerve block applications. Therefore, evaluating videos on platforms that publish educational content, such as YouTube, is essential. Studies in the literature have evaluated educational videos with various types of YouTube content.^{8,12,16} This study is the first to collectively evaluate videos on YouTube related to ten different types of lower extremity nerve blocks. Previous research highlights the importance of YouTube medical education videos containing complete and accurate information.^{8,9,17-19} Studies have emphasized that the quality of YouTube videos is generally low regarding medical content.^{11,14,20} In this study, none of the videos achieved a "perfect" rating based on survey 1 and survey 2, and only two videos were rated as "good." According to survey 1, 23 videos were rated as "bad" and "it will do," while survey 2 rated 11 videos as "bad" and 37 as "it will do." Similar to previous studies, this study demonstrated that YouTube videos were generally not at a sufficient quality level. This finding suggests that although educational videos often meet a certain standard, areas need improvement. Therefore, platforms like YouTube should strive to enhance their quality monitoring processes to ensure users access more reliable, informative, and impactful content. Providing feedback to content providers and encouraging them to produce higher-quality material could be an effective way for platforms to improve content quality. It is essential to guide content creators to convey accurate information on topics that require expertise, such as healthcare, education, and other specialized fields. Studies have reported that sterility is often not emphasized in the videos and that sterility procedures are not adequately explained.^{8,9} This study noted that a significant portion of the evaluated videos needed to explain sterility and

adhere to sterility protocols adequately. Neglecting sterility in nerve block procedures poses serious risks to patient safety. Adhering strictly to sterility standards is crucial for reducing infection risks and achieving optimal clinical outcomes. Healthcare professionals should know the importance of complying with sterility standards through regular training and awareness programs. In this study, it was noted that the videos provided clear anatomical explanations and had good anatomical visuals in terms of educational quality. However, many videos needed a method to evaluate their effectiveness, and the content did not progress step-by-step.

In contrast, the videos were reported to encourage viewers to attempt to block applications moderately. This study demonstrates that the educational and preparation quality of the videos varies, with areas needing improvement. While certain aspects were rated quite well, others received lower scores, indicating the need for revisions in some parts of the videos to achieve a more balanced educational quality.

In this study, the positive correlation between video length and the number of likes with educational and preparation quality suggests that viewers place more trust in longer, detailed content, reflected by higher like counts. This indicates that educational videos offering a certain depth and level of detail are perceived by viewers as more reliable and comprehensive.

The significant positive correlation between educational and preparation quality scores indicates that preparation quality elements, such as sound and visuals, are directly related to content quality. This suggests that when videos are produced according to technical quality standards, the perceived reliability and effectiveness of the content increase. From a technical standpoint, well-prepared videos are likely to be taken more seriously by viewers and positively impact learning processes. This finding emphasizes the importance of content richness and audiovisual quality during the video preparation stage, indicating the need for a comprehensive preparation process to enhance the effectiveness of videos, especially those in educational and professional fields.

Some studies have highlighted a significant relationship between view count and video quality,^{8,9} while other studies have reported no such relationship between view count and video quality.^{14,21} In this study, view count was found to have no significant relationship with quality scores. This suggests that view count may not be an indicator of quality but is likely influenced by other factors, such as video accessibility or popularity.

Limitations

This study analyzed only videos available on YouTube. Other video-sharing platforms also feature educational videos. Excluding videos from other platforms limited access to a broader and more diverse content pool on lower extremity peripheral nerve blocks. Therefore, the study reflects data solely from YouTube and only encompasses potential findings that could be obtained by evaluating educational materials available on other platforms.

CONCLUSION

Lower extremity peripheral nerve blocks are complex regional procedures in the final stages of anesthesiology training,

requiring experience and expertise. Learning such a complex process solely through videos is not feasible; a clinical approach and hands-on practice are essential. While many physicians use social media platforms to enhance their learning and clinical experience, our study suggests they should provide more excellent educational value for lower extremity peripheral nerve blocks. Therefore, we recommend that anesthesiology communities ensure that such educational videos are developed under guidelines and reviewed by experts.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical committee approval was not required because this study did not involve human or animal subjects.

Informed Consent

Informed consent was not required because this study did not involve human or animal subjects.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. YouTube statistics. URL: <https://www.youtube.com/yt/press/statistics.html>.
2. Azer SA, Algrain HA, AlKhelaif RA, AlEshaiwi SM. Evaluation of the educational value of YouTube videos about physical examination of the cardiovascular and respiratory systems. *J Med Internet Res*. 2013;15(11):e241. doi:10.2196/jmir.2728
3. Ng FK, Wallace S, Coe B, et al. From smartphone to bedside: exploring the use of social media to disseminate recommendations from the national tracheostomy safety project to front-line clinical staff. *Anaesthe*. 2020; 75(2):227-233. doi:10.1111/anae.14747
4. Romanov K, Nevgi A. Do medical students watch video clips in eLearning and do these facilitate learning? *Med Teach*. 2007;29(5):484-488. doi:10.1080/01421590701542119
5. Staunton PF, Baker JF, Green J, Devitt A. Online curves: a quality analysis of scoliosis videos on YouTube. *Spine (Phila Pa 1976)*. 2015;40(23):1857-1861. doi:10.1097/BRS.0000000000001137
6. Yildirim B, Basaran O, Alatas OD, et al. Chest tube insertion techniques on YouTube: is social media a reliable source of learning medical skills? *Am J Emerg Med*. 2015;33(11):1709-1710. doi:10.1016/j.ajem.2015.08.040
7. Mueller SM, Jungo P, Cajacob L, Schwegler S, Itin P, Brandt O. The absence of evidence is evidence of non-sense: cross-sectional study on the quality of psoriasis-related videos on YouTube and their reception by health seekers. *J. Med. Int*. 2019;21(1):e11935. doi:10.2196/11935
8. Satici MH. Evaluation of YouTube videos for learning interfascial plane blocks. *Med Records*. 2024;6(3):317-323. doi:10.37990/medr.1475153
9. Satici MH, Tutar MS. Analyzing the educational quality of YouTube videos on paravertebral block techniques. *CJPM*. 2024;2(2):43-54. doi:10.20528/cjpm.2024.02.003
10. Cho NR, Cha JH, Park JJ, Kim YH, Ko DS. Reliability and quality of YouTube videos on ultrasound-guided brachial plexus block: a programmatic review. *In Healthcare*. 2021;9(8):1083. doi:10.3390/healthcare9081083

11. Selvi O, Tulgar S, Senturk O, Topcu DI, Ozer Z. YouTube as an informational source for brachial plexus blocks: evaluation of content and educational value. *Rev Bras Anesthesiol.* 2019;69(2):168-176. doi:10.1016/j.bjan.2018.11.004
12. Turhan S, Ekici AA. YouTube as an information source of transversus abdominis plane block. *Turk J Clin Lab.* 2023;12(2):216-221. doi:10.18663/tjcl.1272291
13. De Cassai A, Correale C, Sandei L, Ban I, Selvi O, Tulgar S. Quality of erector spinae plane block educational videos on a popular video-sharing platform. *Cureus.* 2019;11(3):e4204. doi:10.7759/cureus.4204
14. Tulgar S, Selvi O, Serifsoy TE, Senturk O, Ozer Z. YouTube as an information source of spinal anesthesia, epidural anesthesia and combined spinal and epidural anesthesia. *Rev Bras Anesthesiol.* 2017;67(5):493-499. doi:10.1016/j.bjan.2016.08.007
15. National Career Development Association (NCDA) guidelines for the preparation and evaluation of video career media. (2019). Accessed: 18.02.2019: <https://www.ncda.org/aws/NCDA/asset manager/getfile/340>.
16. Arslan B, Sugur T, Ciloglu O, Arslan A, Acik V. A cross-sectional study analyzing the quality of YouTube videos as a source of information for COVID-19 intubation. *Braz J Anesthesiol.* 2022;72(2):302-305. doi:10.1016/j.bjane.2021.10.002
17. Gonzalez-Estrada A, Cuervo-Pardo L, Ghosh B, et al. Popular on YouTube: a critical appraisal of the educational quality of information regarding asthma. *Allergy Asthma Proc.* 2015;36(6):121-126. doi:10.2500/aap.2015.36.3890
18. Turhan VB, Ünsal A. Evaluation of the quality of videos on hemorrhoidal disease on YouTube™. *Turk J Colorectal Dis.* 2021;31(3):261-267. doi:10.4274/tjcd.galenos.2021.2021-1-4
19. Tewfik GL, Work AN, Shulman SM, Discepola P. Objective validation of YouTube™ educational videos for the instruction of regional anesthesia nerve blocks: a novel approach. *BMC Anesthesiol.* 2020;20(1):1-7. doi:10.1186/s12871-020-01084-w
20. Nason K, Donnelly A, Duncan HF. YouTube as a patient-information source for root canal treatment. *Int Endod J.* 2016;49(12):1194-1200. doi:10.1111/iej.12575
21. Tackett S, Slinn K, Marshall T, Gaglani S, Waldman V, Desai R. Medical education videos for the world. An analysis of viewing patterns for a YouTube channel. *Acad Med.* 2018;93(8):1150-1156. doi:10.1097/ACM.0000000000002118

Examining the effects of lidocaine and dexmedetomidine on compound action potential in rat sciatic nerve

 Hatice Toprak¹,  Cemile Öztin Ögün²

¹Department of Anesthesiology and Reanimation, Faculty of Medicine, Karamanoğlu Mehmetbey University, Karaman, Türkiye

²Anesthesiology and Reanimation Specialist, Dr. Getat Clinic, Konya, Türkiye

Cite this article: Toprak H, Öztin Ögün C. Examining the effects of lidocaine and dexmedetomidine on compound action potential in rat sciatic nerve. *Eur J Anesthesiol Intens Care*. 2025;2(1):18-23.

Corresponding Author: Hatice Toprak, dr.tprk@hotmail.com

Received: 22/11/2024

Accepted: 27/12/2024

Published: 03/02/2025

ABSTRACT

Aims: Recent interest in peripheral regional blocks (PRB) has increased for surgical and nonsurgical implementations. Lidocaine is frequently preferred in PRBs because of its wide safety margin. The short duration of action limits the use of lidocaine. Dexmedetomidine is a new-generation adjuvant agent. According to our hypothesis, dexmedetomidine will prolong the duration of the action of lidocaine.

Methods: A total of 48 rat sciatic nerves were isolated and electrophysiological recordings were taken from 28. They were then randomly divided into 4 groups as group control (C), group L given 1 mM lidocaine, group D given 5 microgram/L dexmedetomidine, and group LD given 1 mM Lidocaine and 5 microgram/L dexmedetomidine. Compound action potentials (CAP) were recorded after the stimulation of the nerves. Maximum depolarization value (MD, mV), time to maximum depolarization (MDT), Area Under the CAP curve (Area, mV.ms), and conduction velocities were calculated separately for fast-conducting fibers (CVF, m/s) and medium-slow-conducting fibers (CVM, m/s).

Results: No significant effects of dexmedetomidine was detected compared to the control group for all comparisons ($p>0.05$). In the area under the curve evaluations that provide information on the number of affected fibers, a statistically significant difference was detected in group LD compared to group C ($p=0.001$). A statistically significant difference was detected in the nerve conduction velocity evaluations between group LD and group L in fast conduction velocity and medium and slow conduction velocity fibers ($p=0.002$, $p=0.009$ for fast conducting fibers and medium and slow conducting fibers, respectively).

Conclusion: When nerve conduction parameters were evaluated, dexmedetomidine alone did not exhibit a significant effect. When applied with lidocaine, it increased the effects of lidocaine on nerve conduction parameters and decreased nerve conduction velocities. Our results showed that dexmedetomidine interacts additively or synergistically with lidocaine and prolongs the duration of effect of lidocaine.

Keywords: Rat sciatic nerves, compound action potentials, lidocaine, dexmedetomidine

INTRODUCTION

Peripheral regional blocks (PRBs) are the administration of nerve inhibitory drugs (primarily local anesthetics) to the area around a specific nerve or nerve bundle¹, distal to the needle site to provide anesthesia.² PRBs are often preferred for patients who have a high risk of postoperative respiratory depression after general anesthesia, such as advanced age, severe obesity, obstructive sleep disorders, and acute or chronic lung diseases. In recent years, PRBs have been frequently included in multimodal analgesia regimens aimed at restricting opioid use.^{3,4} When applied correctly and effectively, PRBs can

provide better analgesia than opioids.⁵ The widespread use of ultrasonography continues to contribute to the development of PRB techniques.

Local anesthetics (LA) are administered to the nerve periphery by single-shot or continuous injection methods in PRBs.⁶ Continuous injection techniques have been associated with adverse conditions such as nerve damage, difficulty in catheter removal, infection, injection catheter displacement, local anesthetic systemic toxicity (LAST), and neurotoxicity.^{4,7} The duration of benefit of single-shot PRBs is associated with the

duration of the LA effect, and strategies that will contribute to prolonging this duration are being investigated. The use of adjuvant drugs is one of the strategies applied to prolong the duration of the effect of single-shot PRBs.⁸

Lidocaine is one of the oldest and most commonly used LAs. The reason for the interest in lidocaine might be its long-term use, clinicians' habits, trust, and short onset of action. As well as these advantages, Lidocaine may also increase the cytolytic activity of natural killer (NK) cells⁹, improve microvascular perfusion¹⁰, and reduce opioid consumption.¹¹ Its disadvantages are considered to be short duration of action¹², neurotoxicity¹³, and association with LAST.¹⁴ Researchers are encouraged to work on adjuvant agents that aim to decrease the disadvantages of lidocaine.

Dexmedetomidine is one of the novel adjuvant agents that has attracted attention in recent years⁸ as a selective α_2 -adrenergic receptor agonist that can provide analgesia, anti-anxiety, sympathetic system inhibition, mild respiratory inhibition and has little effect on hemodynamic stability.¹⁵ Previous studies reported that the use of dexmedetomidine as an adjuvant agent in PRBs shortens the onset of anesthesia and prolongs the duration of sensory and motor blockade.^{16,17} Various theories were put forward as to how dexmedetomidine exerts these effects. However, its mechanism of action has not been fully elucidated. The peripheral effect is among the strong mechanisms proposed⁴, which may occur because dexmedetomidine maintains the cells in a depolarized state^{18,19} or by delaying the absorption of LA through its vasoconstrictor effect in blood vessels close to the peripheral nerve.^{4,20}

Compound action potentials (CAPs) are the sum of single-fiber action potentials from all fibers in a nerve.²¹ They are obtained by recording the depolarization of a motor nerve after stimulation.²² The rat sciatic nerve has nerve fibers that have different conduction velocities and sensory and motor nerve fibers.^{23,24} CAPs recorded after stimulation of the nerve provide information about the activities of sensory and motor fibers with different conduction velocities.²³ In the present study, the CAP recordings were examined on the rat sciatic nerve to investigate the effects of using dexmedetomidine as an adjuvant agent. According to the hypothesis established here, dexmedetomidine, which is of interest as a new adjuvant, will prolong the effect of lidocaine.

METHODS

This article was produced based on a thesis that was completed in 2012. Approval was obtained from the Selçuk University Experimental Research and Application Center (SUDAM) Experimental Animal Ethics Committee (Date: 28.11.2011, Decision No: 2011-123). Experiments were performed in the laboratories of the Biophysics Department of the Selçuk University Meram Medical Faculty. Surgical and experimental procedures were applied to rats obtained from the Selçuk University Experimental Medical Research and Application Center. The rules determined by the Selçuk University Meram Medical Faculty Experimental Animal Ethics Committee were followed in these procedures.

A total of 24 Wistar albino adult female rats weighing 200-300 g were used in the study. These rats had not been included in any previous study and were not exposed to any drug. Rats whose food and water needs were met and who were provided with

appropriate temperature ($22\pm 2^\circ\text{C}$) and humidity conditions were used in the experiments.

The rats were divided randomly into 4 groups as group C (Control) which was not given any drug, group L (1 mM lidocaine), group D (5 microgram/L dexmedetomidine), and group LD (1 mM lidocaine and 5 microgram/L dexmedetomidine). Anesthesia was induced in the rats with intraperitoneal 100 mg/kg ketamine and 5 mg/kg xylazine. The sciatic nerve was carefully isolated from the left hind leg of each rat. The sciatic nerves were taken to the nerve chamber containing Krebs solution (pH 7.4, 20 mM NaHCO_3 , 10 mM glucose, 119 mM NaCl, 1.2 mM MgSO_4 , 4.8 mM KCl, 1.8 mM CaCl_2 , 1.2 mM KH_2PO_4). The nerves were rested for 5 minutes, drug implementations were made, and CAP recordings were taken after 20 minutes. Supramaximal square pulses were given from the proximal end of the nerve and the distal end was placed in the electrode to transfer the CAP recordings to the computer. Supramaximal square pulses were applied from the proximal end of the nerve with a GrassSIU5 stimulus isolation unit with a Grass S88 stimulator at a frequency of 1 Hz and was repeated for 200 microseconds. CAP recordings were converted to digital data with an Analog/Digital converter (AdvantechPCL-717 A/D Converter) and transferred to the computer for further analysis. From the CAP recordings, the maximum depolarization value (MD, mV), the area under the CAP curve (Area, mV.ms), and conduction velocities were calculated separately for fast-conducting fibers (CVF) and medium-slow-conducting fibers (CVM).

Primary Outcome

To examine the effects of lidocaine and dexmedetomidine separately on CAP potentials in the rat sciatic nerve.

Secondary Outcome

To examine the contribution of dexmedetomidine to the local anesthetic efficacy of lidocaine when used as an adjuvant agent.

Statistical Analysis

The SPSS 16.0 (SPSS IL 16.0 Chicago, USA) package program was used to evaluate the recorded data. The difference between the data obtained from the experimental groups was evaluated by one-way analysis of variance (ANOVA). The Tukey Multiple Comparison Test was used between the parameters where the difference between the groups was significant ($p < 0.05$). It was found that the groups differed from each other at a 95% Confidence Interval. The difference between the groups less than $p < 0.05$ was accepted as statistically significant. All experimental parameters are given as mean $\pm$ standard error throughout the text.

RESULTS

The study was conducted in the Nerve Electrophysiology Laboratories of the Department of Biophysics of the Meram Medical Faculty of Necmettin Erbakan University. 48 sciatic nerves were isolated from 24 rats included in the study. Electrophysiological recordings of 28 sciatic nerves could be used for the study. Nerves that were crushed during their removal and placement for recording were not included in the study.

The data of the control group (C), lidocaine (L) group, dexmedetomidine (D) group and lidocaine+dexmedetomidine

(LD) Group were compared for MD, time to maximum depolarization (MDT), conduction velocity of CVF, conduction velocity of CVM and area under the curve (Area) (Table 1). The differences between the groups were found to be significant for all data ($p < 0.05$).

The highest peak of CAPs during depolarization was defined as MD. The groups were compared for MDs (Table 2). In the comparisons of MD values between groups, significant differences were detected for the control group, group L, and group LD ($p = 0.000$). Significant differences were detected between group L and group D ($p = 0.000$). However, there was no significant difference between group L and group LD. MDT was defined as the time from the moment the stimulation was given from the proximal end of the rat sciatic nerve to the time MD was reached. In the comparisons of MDT values between groups, significant differences were detected for group C and group LD ($p = 0.000$). Also, significant differences were detected between group L and group D ($p = 0.000$). However, there was no significant difference between group L and group LD (Table 3).

For field evaluations, the areas under the curve of the recorded CAPs were calculated as a parameter associated with the depth of sensory and motor blockade. In the comparison of the area under the curve values between the groups, significant differences were detected for group C and group LD ($p = 0.001$). This result may show that the highest difference for the area under the curve was achieved with the LD group (Table 4).

The data on conduction velocities of CVF with CAP recordings were defined as CVF, which was calculated based on the time from the moment the stimulus was given from the proximal

end of the rat sciatic nerve to the moment of CAP onset. In the comparison of CVF values between the groups, significant differences were detected for the control group, group L, and group LD ($p = 0.007$, $p = 0.000$, respectively). Significant differences were detected between group L and group D and group LD ($p = 0.002$, $p = 0.002$, respectively). Significant differences were detected between group D and group LD ($p = 0.000$). This result may show us that lidocaine is effective on CVF and that it is effective on CVF when applied with dexmedetomidine (Table 5).

The data on conduction velocities of medium and slow conducting fibers with CAP recordings were defined as CVM, which was calculated based on the time from the moment the stimulus was given from the proximal end of the rat sciatic nerve until reaching MD. In the comparison of CVM values between the groups, significant differences were detected for the control group, group L, and group LD ($p = 0.000$, $p = 0.000$, respectively). Significant differences were detected between group L, group D, and group LD ($p = 0.000$, $p = 0.009$, respectively). Significant differences were detected between group D and group LD ($p = 0.000$). This result may show us that lidocaine is effective on CVF, and when applied with dexmedetomidine, it is effective on fibers with medium and slow conduction velocities (Table 6).

DISCUSSION

In the present study, the effects of perineural lidocaine and dexmedetomidine on CAP recordings in rat sciatic nerve were investigated when applied alone and together and it was found that dexmedetomidine reduces the conduction velocity of fibers

Table 1. Comparison of parameters between groups (mean $\pm$ SD)

	Group C (n=6)	Group L (n=6)	Group D (n=6)	Group LD (n=6)	p
MD (mV)	9.00 $\pm$ 1.33 (8.08-11.89)	3.92 $\pm$ 1.15 (2.83-6.12)	8.59 $\pm$ 2.31 (6.70-13.57)	1.97 $\pm$ 1.05 (0.60-3.96)	<0.05*
MDT (ms)	0.20 $\pm$ 0.03 (0.18-0.28)	0.36 $\pm$ 0.11 (0.26-0.60)	0.17 $\pm$ 0.02 (0.16-0.22)	0.45 $\pm$ 0.05 (0.38-0.56)	<0.05*
Area (mVxms)	3.26 $\pm$ 0.52 (2.39-4.00)	2.65 $\pm$ 0.38 (2.17-3.32)	3.64 $\pm$ 0.89 (2.85-5.51)	1.67 $\pm$ 0.77 (0.55-3.03)	<0.05*
Conduction velocity of fast conductive fibers (CVF) (m/s)	46.29 $\pm$ 5.39 (38.46-52.63)	37.11 $\pm$ 4.34 (30.30-41.66)	47.73 $\pm$ 4.53 (40.00-52.63)	26.88 $\pm$ 4.55 (20.00-34.48)	<0.05*
Conduction velocity of medium-slow conductive fibers (CVM) (m/s)	31.63 $\pm$ 3.58 (25.00-35.71)	22.45 $\pm$ 3.67 (15.87-26.31)	33.28 $\pm$ 2.10 (30.30-37.03)	16.73 $\pm$ 2.43 (12.82-20.83)	<0.05*

SD: Standard deviation, MD: Maximum depolarization, MDT: Time to reach maximum depolarization, Area: Area under the curve, CVF: Conduction velocity of fast conductive fibers, CVM: Conduction velocity of medium-slow conductive fibers. * p value is below the threshold of <0.05

Table 2. Comparison of maximum depolarization values between groups

	Group C Group L	Group C Group D	Group C Group LD	Group L Group D	Group L Group LD	Group D Group LD
MD (mV)	9.00 $\pm$ 1.33	9.00 $\pm$ 1.33	9.00 $\pm$ 1.33	3.92 $\pm$ 1.15	3.92 $\pm$ 1.15	8.59 $\pm$ 2.31
	3.92 $\pm$ 1.15	8.59 $\pm$ 2.31	1.97 $\pm$ 1.05	8.59 $\pm$ 2.31	1.97 $\pm$ 1.05	1.97 $\pm$ 1.05
p	0.000*	0.961	0.000*	0.000*	0.112	0.000*

MD: Maximum depolarization, * p value is below the threshold of <0.05

Table 3. Comparison of the groups for the time to reach maximum depolarization

	Group C Group L	Group C Group D	Group C Group LD	Group L Group D	Group L Group LD	Group D Group LD
MDT (ms)	0.20 $\pm$ 0.03	0.20 $\pm$ 0.03	0.20 $\pm$ 0.03	0.36 $\pm$ 0.11	0.36 $\pm$ 0.11	0.17 $\pm$ 0.02
	0.36 $\pm$ 0.11	0.17 $\pm$ 0.02	0.45 $\pm$ 0.05	0.17 $\pm$ 0.02	0.45 $\pm$ 0.05	0.45 $\pm$ 0.05
p	0.001	0.885	0.000*	0.000*	0.100	0.000*

MDT: Time to reach maximum depolarization, * p value is below the threshold of <0.05

Table 4. Comparison of groups for area under the CAP curve

	Group C Group L	Group C Group D	Group C Group LD	Group L Group D	Group L Group LD	Group D Group LD
Area (mVxms)	3.26±0.52	3.26±0.52	3.26±0.52	2.65±0.38	2.65±0.38	3.64±0.89
	2.65±0.38	3.64±0.89	1.67±0.77	3.64±0.89	1.67±0.77	1.67±0.77
p	0.354	0.714	0.001*	0.051	0.056	0.000*

* p value is below the threshold of <0.05, CAP: Compound action potentials

Table 5. Comparison of groups for CVF

	Group C Group L	Group C Group D	Group C Group LD	Group L Group D	Group L Group LD	Group D Group LD
CVF (m/s)	46.29±5.39	46.29±5.39	46.29±5.39	37.11±4.34	37.11±4.34	47.73±4.53
	37.11±4.34	47.73±4.53	26.88±4.55	47.73±4.53	26.88±4.55	26.88±4.55
p	0.007*	0.940	0.000*	0.002*	0.002*	0.000*

CVF: The velocity of fibers with fast conduction velocity * p value is below the threshold of <0.05

Table 6. Comparison of groups for CVM

	GroupC Group L	Group C Group D	Group C GroupLD	Group L Group D	Group L GroupLD	Group D Group LD
CVM (m/s)	31.63±3.58	31.63±3.58	31.63±3.58	22.45±3.67	22.45±3.67	33.28±2.10
	22.45±3.67	33.28±2.10	16.73±2.43	33.28±2.10	16.73±2.43	16.73±2.43
P	0.000	0.740	0.000	0.000	0.009	0.000

CVM: Conduction velocity of medium-slow conductive fibers, * p value is below the threshold of <0.05

with both fast and medium and slow conduction velocities. These results may show that dexmedetomidine shortens the onset of the block and prolongs the duration of the block when applied with lidocaine as an adjuvant agent. MD value and area under the curve are proportional to the number of nerve fibers stimulated in that nerve.²³ Although not statistically significant in the present study, a greater decrease was observed in group LD compared to group L for MD value. This result may indicate that dexmedetomidine provides blockade of more nerve fibers when used with lidocaine. The other result showing blockade of more nerve fibers with dexmedetomidine added to lidocaine is the decrease in the area under the curve. When compared with group C, a statistically significant difference was shown only in group LD. This may indicate that the number of fibers developing block increased in group LD and that dexmedetomidine deepened the blockade caused by lidocaine.

The conduction speed of fibers with fast conduction speed is determined by the time from the moment when the stimulus is applied from the proximal end of the rat sciatic nerve to the moment when the CAP is started. In fibers that have medium and slow conduction speeds, the conduction speed is determined by the time from the moment when the stimulus is given from the proximal end of the rat sciatic nerve to the moment when the MD is reached.²⁵ In our study, the specified times were prolonged in each fiber group. The CVF and CVM values between group L and group LD are statistically significant. However, the difference is greater in CVF. This shows the conduction speed of CVF. Our results are consistent with the findings of the previously presented study.²³ Our results may show that the effect of dexmedetomidine is stronger in fibers with fast conduction speed when added to lidocaine. In previous clinical studies, clinical data were presented indicating that dexmedetomidine shortens the onset time of the block and prolongs the block duration.¹⁶ It has been reported that dexmedetomidine added to perineural ropivacaine in the canine sciatic nerve increases the duration

of sensory block.²⁶ The decrease we found in CVF and CVM supports the fact that dexmedetomidine shortens the time to onset of the block and prolongs the duration of the block when applied as an adjuvant agent.

Dexmedetomidine was reported to increase the effect of LA in a dose-dependent manner in previous studies.²⁷ Kosugu et al.²⁸ examined the CAPs recorded from frog sciatic nerves by different adrenoceptor agonists, including dexmedetomidine, and reported that dexmedetomidine reduced the CAP peak amplitude at high concentrations and that this effect was reversible.

The mechanism of action of dexmedetomidine, which is a selective α_2 -adrenergic receptor agonist, on ion channels and membrane potentials has not been fully elucidated. Previous studies speculated that dexmedetomidine might have effects on different ion channels. Chen et al.²⁹ reported evidence that dexmedetomidine had effects on sodium and potassium channels in differentiated neurons. Ishii et al.³⁰ argued that dexmedetomidine hyperpolarizes membrane potentials in spinal dorsal horn neurons through G-protein-mediated activation of K^+ channels. Oda et al.³¹ reported that dexmedetomidine suppresses voltage-gated Na^+ channel currents together with lidocaine, and creates an additive effect when used in regional anesthesia. In the present study, it was found that dexmedetomidine had no significant effects on rat sciatic nerve membrane potentials when applied alone. However, it increased the effects of lidocaine when used with lidocaine. Our findings are consistent with the results of Dalkılıç et al.'s³² study. Our results support the opinion that dexmedetomidine provides its additive or synergistic effect when used with lidocaine through its effect on ion channels.

It is already known that conduction velocity increases with fiber diameter³³ and myelin thickness.^{34,35} Previous studies reported that clonidine, which is an α_2 agonist like dexmedetomidine, inhibits CAP amplitude and that this inhibition is dominant on myelinated A α and unmyelinated C fibers.^{36,37} The fact that the

effect on CVF is greater in the results of our study suggests that type A fibers may have been affected more.

The use of dexmedetomidine as an adjuvant agent in PRBs was evaluated previously in clinical studies. Ghaderi et al.³⁸ reported that they created a longer sensory block by adding dexmedetomidine to lidocaine in forearm Bier block applications. Hu et al.³⁹ argued that perineural dexmedetomidine added to lidocaine and ropivacaine provided a faster onset time and a longer duration of effect in popliteal block. Abdullatif et al.⁴⁰ reported that perineural dexmedetomidine shortened the onset time of bupivacaine-induced femoral nerve block and prolonged the duration of block. The possibility that perineural dexmedetomidine passes into the systemic circulation cannot be excluded in clinical studies. It is important to demonstrate the effects of dexmedetomidine on membrane potentials. Our results can be considered as an experimental study supporting the clinical studies that evaluated the use of dexmedetomidine as an adjuvant agent in PRBs in the literature.

Lidocaine blocks voltage-gated sodium channels¹³ and is not used only as LA. Systemic Lidocaine has antinociceptive effects in acute and chronic pain. These effects cannot be explained solely by its voltage-gated sodium channel-blocking properties, but the responsible mechanisms are still unclear.³² Recently, clinicians have shown great interest in PRBs, especially fascial plane blocks, and, likely, PRBs are widely used with systemic lidocaine¹⁴, which may be associated with increased LAST. One of the interventions aimed at limiting the use of Lidocaine in high-dose PRBs is the use of dexmedetomidine as an adjuvant agent.

Limitations

The small number of experimental animals in our study is our limitation. In the present study, not evaluating the dose and concentration differences of the agents, not evaluating their reversibility, and not being able to present data associated with neurotoxicity were considered as limitations.

The peripheral and systemic mechanisms of action of lidocaine and dexmedetomidine and their relationships with each other have not been fully explained. We believe that our study provides important findings for future studies. Considering the increasing PRBs, we believe that studies on dexmedetomidine and lidocaine will be presented in the literature in the future.

CONCLUSION

The study was conducted to evaluate the hypothesis that dexmedetomidine would prolong the duration of lidocaine effect when added to lidocaine. As a result of the study, it was found that dexmedetomidine could achieve the block duration achieved with lidocaine by slowing down conduction velocities. As an experimental study, the present research contributed and supported clinical studies concluding that dexmedetomidine prolongs the duration of sensory and motor block when added to lidocaine as a perineural adjuvant agent. To support our results and improve safety and clinical outcomes, studies using more experimental animals to eliminate our limitations are needed. In conclusion, this study provides important contributions that dexmedetomidine increases the effects of lidocaine when used perineurally with lidocaine.

ETHICAL DECLARATIONS

Ethics Committee Approval

Approval was obtained from the Selçuk University Experimental Research and Application Center (SUDAM) Experimental Animal Ethics Committee (Date: 28.11.2011, Decision No: 2011-123).

Informed Consent

As this study is an animal experiment, informed consent is not required.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Acknowledgments

The present study was prepared based on the specialization thesis "Examining the Effect of Dexmedetomidine on Lidocaine-Induced Changes in Isolated Rat Sciatic Nerve Electrophysiological Parameters", which we completed in 2012 under the supervision of Prof. Dr. Cemile Öztin Ögün. The study was conducted in the Laboratory of Biophysics Department of the Faculty of Medicine of Necmettin Erbakan University. We would like to thank Nizamettin Dalkılıç and Seçkin Tuncer for their efforts in obtaining and interpreting the records in the biophysics laboratory.

REFERENCES

1. Wu D, Patil A. Minimising complications and improving the success of peripheral regional blockade. *Br J Hosp Med.* 2022;83(10):1-10. doi:10.12968/hmed.2022.0304
2. Fallon F, Moorthy A, Skerritt C, Crowe GG, Buggy DJ. Latest Advances in regional anaesthesia. *Medicina (Mex).* 2024;60(5):735. doi:10.3390/medicina60050735
3. Lee HH, Kwon HM, Lee WS, Yang IH, Choi YS, Park KK. Effectiveness of ERAS (enhanced recovery after surgery) protocol via peripheral nerve block for total knee arthroplasty. *J Clin Med.* 2022;11(12):3354. doi:10.3390/jcm11123354
4. Chen Z, Liu Z, Feng C, Jin Y, Zhao X. Dexmedetomidine as an adjuvant in peripheral nerve block. *Drug Des Devel Ther.* 2023;17:1463-1484. doi:10.2147/DDDT.S405294
5. Hopkins PM. Does regional anaesthesia improve outcome? *Br J Anaesth.* 2015;115(Suppl 2):ii26-ii33. doi:10.1093/bja/aeu377
6. Ae B, R F, Ji H, Ms A. Continuous peripheral nerve block compared with single-injection peripheral nerve block: a systematic review and meta-analysis of randomized controlled trials. *Reg Anesth Pain Med* [Internet]. 2012 Dec [cited 2024 Nov 2];37(6). Available from: <https://pubmed.ncbi.nlm.nih.gov/23080349/>
7. Ilfeld BM. Continuous peripheral nerve blocks: an update of the published evidence and comparison with novel, alternative analgesic modalities. *Anesth Analg.* 2017;124(1):308-335. doi:10.1213/ANE.0000000000001581
8. Desai N, Kirkham KR, Albrecht E. Local anaesthetic adjuncts for peripheral regional anaesthesia: a narrative review. [cited 2024 Jul 24]; Available from: <https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.15245>

9. Cata JP, Ramirez MF, Velasquez JF, et al. Lidocaine stimulates the function of natural killer cells in different experimental settings. *Anticancer Res.* 2017;37(9):4727-4732. doi:10.21873/anticancer.11879
10. Grotowska M, Gozdzik W. Intraoperative intravenous infusion of lidocaine increases total and small vessel densities of sublingual microcirculation: a randomized prospective pilot study. *J Int Med Res.* 2023;51(11):3000605231209820. doi:10.1177/03000605231209820
11. Karlsdottir BR, Zhou PP, Wahba J, et al. Male gender, smoking, younger age, and preoperative pain found to increase postoperative opioid requirements in 592 elective colorectal resections. *Int J Colorectal Dis.* 2022;37(8):1799-1806. doi:10.1007/s00384-022-04208-5
12. Choi GJ, Ahn EJ, Lee OH, Kang H. Effects of a BMI1008 mixture on postoperative pain in a rat model of incisional pain. *PLoS ONE.* 2021;16(9):e0257267. doi:10.1371/journal.pone.0257267
13. Moldovan M, Lange KHW, Aachmann-Andersen NJ, Kjær TW, Olsen NV, Krarup C. Transient impairment of the axolemma following regional anaesthesia by lidocaine in humans. *J Physiol.* 2014;592(Pt 13):2735. doi:10.1113/jphysiol.2014.270827
14. Shanthanna H, Weinberg G. Intravenous lidocaine, regional blockade, or both: considerations for multiple interventions involving local anaesthetics. *Br J Anaesth.* 2021;127(4):497-501. doi:10.1016/j.bja.2021.04.024
15. Bilotta F, Pugliese F. The evolving clinical use of dexmedetomidine. *The Lancet.* 2020;396(10245):145-147. doi:10.1016/S0140-6736(20)30902-8
16. Singh N, Gupta S, Kathuria S. Dexmedetomidine vs dexamethasone as an adjuvant to 0.5% ropivacaine in ultrasound-guided supraclavicular brachial plexus block. *J Anaesthesiol Clin Pharmacol.* 2020;36(2):238. doi:10.4103/joacp.JOACP_176_19
17. Rancourt MP, Albert NT, Côté M, Létourneau DR, Bernard PM. Posterior tibial nerve sensory blockade duration prolonged by adding dexmedetomidine to ropivacaine. *Anesth Analg.* 2012;115(4):958. doi:10.1213/ANE.0b013e318265bab7
18. Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. *Anesthesiology.* 2011;115(4):836-843. doi:10.1097/ALN.0b013e318221fcc9
19. Kroin JS, Buvanendran A, Beck DR, Topic JE, Watts DE, Tuman KJ. Clonidine prolongation of lidocaine analgesia after sciatic nerve block in rats is mediated via the hyperpolarization-activated cation current, not by α -adrenoreceptors. *Anesthesiology.* 2004;101(2):488-494. doi:10.1097/00000542-200408000-00031
20. Han M, Kang F, Yang C, et al. Comparison of adrenaline and dexmedetomidine in improving the cutaneous analgesia of mexiletine in response to skin pinpricks in rats. *Pharmacology.* 2020;105(11-12):662-668. doi:10.1159/000506487
21. Peña E, Pelot NA, Grill WM. Computational models of compound nerve action potentials: efficient filter-based methods to quantify effects of tissue conductivities, conduction distance, and nerve fiber parameters. *PLOS Comput Biol.* 2024;20(3):e1011833. doi:10.1371/journal.pcbi.1011833
22. Barrois R, Barnerias C, Deladrière E, et al. A new score combining compound muscle action potential (CMAP) amplitudes and motor score is predictive of motor outcome after AVXS-101 (Onasemnogene Apeparvovec) SMA therapy. *Neuromuscul Disord.* 2023;33(4):309-314. doi:10.1016/j.nmd.2023.02.004
23. Taylan SB, Bariskaner H. Effects of dexmedetomidine and dexketoprofen on the conduction block of rat sciatic nerve. *Neural Regen Res.* 2020;15(5):929. doi:10.4103/1673-5374.268926
24. Kincaid JC, Minnick KA, Pappas S. A model of the differing change in motor and sensory action potentials over distance. *Muscle Nerve.* 1988;11(4):318-323. doi:10.1002/mus.880110407
25. Dalkılıç N, Pehlivan F. Comparison of fiber diameter distributions deduced by modeling compound action potentials recorded by extracellular and suction techniques. *Int J Neurosci.* 2002;112(8):913-930. doi:10.1080/00207450290025923
26. Marolf V, Ida KK, Siluk D, Struck-Lewicka W, Markuszewski MJ, Sandersen C. Effects of perineural administration of ropivacaine combined with perineural or intravenous administration of dexmedetomidine for sciatic and saphenous nerve blocks in dogs. 2021 Jun 1 [cited 2024 Nov 11]; Available from: <https://avmajournals.avma.org/view/journals/ajvr/82/6/ajvr.82.6.449.xml>
27. Ouchi K, Koga Y, Nakao S, Sugiyama K. Dexmedetomidine dose-dependently enhances local anesthetic action of lidocaine. *J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg.* 2014;72(3):474-480. doi:10.1016/j.joms.2013.09.038
28. Kosugi T, Mizuta K, Fujita T, Nakashima M, Kumamoto E. High concentrations of dexmedetomidine inhibit compound action potentials in frog sciatic nerves without α 2 adrenoceptor activation. *Br J Pharmacol.* 2010;160(7):1662-1676. doi:10.1111/j.1476-5381.2010.00833.x
29. Chen BS, Peng H, Wu SN. Dexmedetomidine, an α 2-adrenergic agonist, inhibits neuronal delayed-rectifier potassium current and sodium current. *Br J Anaesth.* 2009;103(2):244-254. doi:10.1093/bja/aep107
30. Ishii H, Kohno T, Yamakura T, Ikoma M, Baba H. Action of dexmedetomidine on the substantia gelatinosa neurons of the rat spinal cord. *Eur J Neurosci.* 2008;27(12):3182-3190. doi:10.1111/j.1460-9568.2008.06260.x
31. Oda A, Iida H, Tanahashi S, Osawa Y, Yamaguchi S, Dohi S. Effects of α 2-adrenoceptor agonists on tetrodotoxin-resistant Na⁺ channels in rat dorsal root ganglion neurons*. *Eur J Anaesthesiol EJA.* 2007;24(11):934. doi:10.1017/S0265021507000543
32. Dalkılıç N, Tuncer S, Burat I. Dexmedetomidine augments the effect of lidocaine: power spectrum and nerve conduction velocity distribution study. *BMC Anesthesiol.* 2015;15(1):24. doi:10.1186/s12871-015-0009-9
33. Rushton WA. A theory of the effects of fibre size in medullated nerve. *J Physiol.* 1951;115(1):101-122. doi:10.1113/jphysiol.1951.sp004655
34. Waxman SG. Determinants of conduction velocity in myelinated nerve fibers. *Muscle Nerve.* 1980;3(2):141-150. doi:10.1002/mus.880030207
35. Ikeda M, Oka Y. The relationship between nerve conduction velocity and fiber morphology during peripheral nerve regeneration. *Brain Behav.* 2012;2(4):382-390. doi:10.1002/brb3.61
36. Butterworth JF, Strichartz GR. The α 2-adrenergic agonists clonidine and guanfacine produce tonic and phasic block of conduction in rat sciatic nerve fibers. *Anesth Analg.* 1993;76(2):295-301.
37. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of lidocaine on C-fiber action potential. *Anesth Analg.* 1992;74(5):719. doi:10.1213/00000539-199205000-00017
38. Ghaderi K, Rahmani K, Rahmanpanah N, Shami S, Zahedi F, Nasser K. Comparison of lidocaine-dexmedetomidine and lidocaine-saline on the characteristics of the modified forearm Bier block: a clinical trial. *J Anaesthesiol Clin Pharmacol.* 2021;37(4):610-615. doi:10.4103/joacp.JOACP_54_20
39. Hu X, Li J, Zhou R, et al. Dexmedetomidine added to local anesthetic mixture of lidocaine and ropivacaine enhances onset and prolongs duration of a popliteal approach to sciatic nerve blockade. *Clin Ther.* 2017;39(1):89-97.e1. doi:10.1016/j.clinthera.2016.11.011
40. Abdulatif M, Fawzy M, Nassar H, Hasanin A, Ollaek M, Mohamed H. The effects of perineural dexmedetomidine on the pharmacodynamic profile of femoral nerve block: a dose-finding randomised, controlled, double-blind study. *Anaesthesia.* 2016;71(10):1177-1185. doi:10.1111/anae.13603

Retrospective investigation of cases diagnosed with brain death

 Sinem Bayrakçı¹,  Elif Eygi²

¹Department of Intensive Care, Gaziantep City Hospital, Gaziantep, Türkiye

²Department of Anesthesiology and Reanimation, Gaziantep City Hospital, Gaziantep, Türkiye

Cite this article: Bayrakçı S, Eygi E. Retrospective investigation of cases diagnosed with brain death. *Eur J Anesthesiol Intens Care*. 2025;2(1):24-28.

Corresponding Author: Sinem Bayrakçı, drsinembayrakci@gmail.com

Received: 08/11/2024

Accepted: 30/12/2024

Published: 03/02/2025

ABSTRACT

Aims: Early and rapid detection of brain death in intensive care units is important for organ transplantation. This study aimed to evaluate cases diagnosed with brain death.

Methods: The retrospective study was conducted by examining the patients diagnosed with brain death in intensive care units of the city hospital between 06.10.2023 and 01.09.2024. Demographic characteristics of the cases, hospitalization diagnoses, clinics where they received treatment, the time from admission to intensive care and the beginning of clinical suspicion of brain death until the report was prepared, additional tests applied, family organ donation rate, donor rate, and the time from the diagnosis of brain death to cardiac arrest in non-donor cases were recorded.

Results: 33 patients were diagnosed with brain death. The mean age of the cases was 52.1, and 51.6% of them were male (n=17). 57.6% of the cases had no known comorbid diseases (n=19). The intensive care units where the cases were hospitalized were 36.4% anesthesia (n=12) and 36.4% neurosurgery (n=12). The hospitalization diagnosis of the cases was intracranial hemorrhage in 30.4% (n=10) and cerebral infarction in 30.4% (n=10). Digital subtraction angiography was used in 70% (n=23) for additional supporting tests. Organ donation was made by the family in 12.1% of the cases (n=4), and organs were transplanted in 9% of these cases (n=3). The average time from admission to diagnosis of brain death was 6.66 days. The average time from follow-up of patients thought to have brain death to diagnosis of brain death was 2.03 days. The average time from diagnosis of brain death to cardiac arrest was 31.85 hours.

Conclusion: It is very important to diagnose brain death in order to increase the number of organ transplants from cadavers. In patients who may be potential donors, brain death should be determined quickly, and rapid action should be taken after diagnosis, and unnecessary loss of time should be avoided.

Keywords: Brain death, intensive care unit, transplantation

INTRODUCTION

Brain death is the persistent and irreversible loss of all activities of the brain, brain stem, and cerebellum, which are the parts of the central nervous system that remain within the skull. There are three main findings in the clinical diagnosis of brain death: deep coma, brainstem areflexia, and a positive apnea test.¹ The definition of brain death was first made by Mollaret and Goulon² in 1959, and many studies and criteria have been developed since then. The Harvard criteria, published in 1968, expanded the medical definition of brain death and formed the basis of today's definitions.³

In our country, since 02.01.2014, the diagnosis of brain death is decided unanimously by two physicians, one of whom is a

neurologist or neurosurgeon and the other is an anesthesiology and reanimation specialist or intensive care specialist.⁴

The number of patients who develop organ failure and need transplantation is increasing. Developments in transplantation and the increasing number of patients waiting for transplantation make cadaver organ transplantation, and therefore brain death and donor care, very important.⁵

The correct and prompt diagnosis of brain death, monitoring of potential donors, obtaining family consent, quality of donor care, and careful management of organ harvesting are essential for an efficient transplantation. Intensive care units play a very important role at this stage. In this study, the characteristics

of brain death cases that occurred in the last 11 months in the city hospital, the supporting tests used in the diagnosis of brain death, and the organ donation acceptance rates of families were examined.

METHODS

The study was conducted with the permission of the Scientific Researches Evaluation and Ethics Committee of Gaziantep City Hospital (Date: 16.10.2024, Decision No: 62/2024), a retrospective study was conducted by examining the archive records of adult and pediatric patients diagnosed with brain death in intensive care units of the city hospital between 06.10.2023 and 01.09.2024. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Patients who were diagnosed with brain death at the end of the follow-up period were included in the study. Patients whose diagnosis process could not be completed or who exited before the necessary procedures were excluded from the study.

Demographic characteristics of the cases, such as age, gender, blood type, comorbid diseases, hospitalization diagnoses, clinics where they received treatment, the time from admission to intensive care and the beginning of clinical suspicion of brain death until the report was prepared, additional tests applied, family organ donation rate, donor rate, and the time from the diagnosis of brain death to cardiac arrest in non-donor cases, were recorded. The data were accessed by examining archive files and computer records. All brain death cases between the dates specified above were included in the study, and cases outside this date range were excluded from the study.

Statistical Analysis

Statistical analyses of the obtained data were performed using SPSS 20.0 (Chicago IL, USA). The Kolmogorov-Smirnov test was used for homogenization of the obtained data. Statistical analysis of homogeneous randomized independent groups would be performed using the Chi-Square Test. Descriptive statistics of the study data were expressed as mean±standard deviation for quantitative data and frequency and percentage values for qualitative data. In the results obtained from the applied statistical tests, p-value below 0.05 and CI 95% were considered statistically significant.

RESULTS

Between 06.10.2023 and 01.09.2024, the total number of adult/pediatric intensive care patients was 1393, the total number of patients followed up with suspicion of brain death was 225, and the number of patients followed up with suspicion of brain death but not diagnosed with brain death was 193. Between 06.10.2023 and 01.09.2024, 33 patients diagnosed with brain death in our hospital were examined. Demographic and clinical data of the patients are shown in [Table 1](#). The mean age of the cases was 52.1, and 51.6% of them were male (n=17). While 57.6% of the cases had no known comorbid diseases (n=19), 24.4% had hypertension (n=8), 9% had coronary artery disease (n=3), 6% had diabetes mellitus (n=2), and 3% had other diseases (n=1). When the blood types of the cases were examined, the majority were group A (36.4%), and 87.8% were Rh positive according to the Rh groups. The intensive care units where the cases were hospitalized were 36.4% anesthesia (n=12), 36.4% neurosurgery (n=12), 9%

Table 1. Demographic data and characteristics of patients

	n (33)	%
Age(years)	52.1±13.3	
Gender (%)		
Male	17	51.6%
Female	16	48.4%
Comorbidity (%)		
None	19	57.6%
Hypertension	8	24.4%
Diabetes mellitus	2	6%
Coronary artery disease	3	9%
Other	1	3%
Blood group (%)		
A	12	36.4%
B	7	21.2%
AB	3	9%
O	11	33.4%
Rh		
Positive	29	87.8%
Negative	4	12.2%
Intensive care unit (%)		
Anesthesia and reanimation	12	36.4%
Neurosurgery	12	36.4%
Neurology	3	9%
Surgical	2	6%
Internal medicine	2	6%
Cardiovascular surgery	2	6%
Admission diagnoses (%)		
Cerebral infarction	10	30.4%
Intracranial hemorrhage	10	30.4%
Traumatic brain injury	6	18.1%
Brain tumor	4	12.1%
Other diseases	3	9%
Nationality (%)		
Turkish	28	84.8%
Other	5	15.2%
Transplantation (%)		
Donation	4	12.1%
Transplant	3	9%
Auxiliary tests used in diagnosis (%)		
None	1	3%
CT angiography	9	27%
DSA	23	70%

CT angiography: Computed tomography angiography, DSA: Digital subtraction angiography

neurology (n=3), 6% surgery (n=2), 6% internal medicine (n=2), and 6% cardiovascular surgery intensive care (n=2). The hospitalization diagnosis of the cases was intracranial hemorrhage in 30.4% (n=10), cerebral infarction in 30.4% (n=10), traumatic brain injury in 18.1% (n=6), brain tumor in 12.1% (n=4), and other diseases in 9% (n=3). While 84.8% of the cases were Turkish (n=28), 15.2% were not citizens of the Republic of Turkey (n=5). Due to apnea test conditions failing to meet in 5 cases (15.15%), brain death was diagnosed with supportive additional testing. While no additional supporting tests were used in 3% of the cases for the diagnosis of brain death (n=1), digital subtraction angiography was used in 70% (n=23), and computerized tomography angiography was used in 27% (n=9). Organ donation was made by the family in 12.1% of the cases (n=4), and organs were transplanted in 9% of these cases (n=3).

The average time from admission to diagnosis of brain death was 6.66 days. The average time from follow-up of patients

thought to have brain death to diagnosis of brain death was 2.03 days. The average time from diagnosis of brain death to cardiac arrest was 31.85 hours (Table 2).

The organs of one case could not be used for medical reasons. In the other three cases, the liver and the right and left kidneys were used for transplantation.

Age, hypertension, Rh-negative blood group, and intracranial hemorrhage diagnosis are statistically associated with the time from admission to the diagnosis of brain death. The time from follow-up to diagnosis of brain death was statistically significantly shorter in cases diagnosed in the anesthesia intensive care unit ($p<0.05$). The time from diagnosis of brain death to cardiac arrest was statistically significantly shorter in patients with coronary artery disease ($p<0.02$) and those diagnosed in the cardiovascular surgery intensive care unit ($p<0.04$). Male gender, absence of comorbid disease, and diagnosis in the anesthesia intensive care unit were statistically significantly associated with donation (Table 3).

DISCUSSION

Similar to the rest of the world, the number of patients waiting for organ transplantation in our country is increasing day by day. For this reason, organ transplantation from a cadaver is of great importance. For organ transplantation from a cadaver, it is important to closely monitor potential donor candidates and diagnose brain death.

In our study, cases diagnosed with brain death between 06.10.2023 and 01.09.2024 were examined. The total number of brain deaths was 33, and the number of organ donations was 4.

In two studies conducted in our country, 70.7% and 61.3% of patients diagnosed with brain death were male, and their mean age was 46.7.^{6,7} In a cohort study conducted on 69,735 cases in the USA, 56.47% of the cases were male, and the average age was 48 years.⁸ The cases in our study were similar to these studies in terms of age and gender.

Table 2. Follow-up processes of cases

	Mean	Median	SD	%95 CI
Time admission-BD (day)*	6.66	5 (1-26)	5.90	2.09
Time follow up-BD (day)**	2.03	2 (0-6)	1.48	0.52
Time BD-cardiac arrest (hour)***	32.67	28 (0-90)	24.25	6.86

*Time from admission to diagnosis of brain death, **Time from start of follow-up to diagnosis of brain death, ***Time from diagnosis of brain death to cardiac arrest, SD: Standard deviation

Table 3. Statistical relationship between demographic data and follow-up processes

	Time admission-BD*	Time follow up-BD**	Time BD-cardiac arrest***	Donation
Age	<0.05			
Gender				
Male				<0.03
Female				
Comorbidity				
None				<0.05
Hypertension	<0.01			
Diabetes mellitus				
Coronary artery disease			<0.02	
Other				
Blood group				
A				
B				
AB				
O				
Rh				
Positive				
Negative	<0.05 (no comorbid)			
Intensive care unit				
Anesthesia		<0.05		<0.05
Neurosurgery				
Neurology				
Surgical				
Internal medicine				
Cardiovascular surgery			<0.04	
Admission diagnoses				
Traumatic brain injury				
Intracranial hemorrhage	<0.05			
Cerebral infarction				
Brain tumor				
Other diseases				
Nationality				
Turkish				
Other				
Transplantation				
Donation				
Transplant				

*Time from admission to diagnosis of brain death, **Time from start of follow-up to diagnosis of brain death, ***Time from diagnosis of brain death to cardiac arrest

In Palabıyık's⁶ study, while there was no comorbid disease in 48.7% of the cases, hypertension (34.1%) was the most common comorbid disease. Similar to Palabıyık's⁶ study, in our study, there was no comorbid disease in 57.6% of the cases, while the most common comorbid disease was hypertension (24.4%). The most common blood group was ARh+ in the study of Eira et al.⁹ ORh+ (41.9%) in the study of Kuşcu et al.⁷ while in our study it was determined as 36.4% A and 87.8% Rh+.

The most common cause of brain death in the cases included in our study was intracranial hemorrhage and cerebral infarction at equal rates. In the studies of Escudero et al.¹¹, Kuşcu et al.⁷, and Karasu et al.¹⁰, the most common cause of brain death was intracranial hemorrhage, while in the study of Karan et al.¹², cerebrovascular events were reported as the most common cause of brain death, and in the study of Akbaş et al.¹³, ischemic stroke was reported as the most common cause of brain death.

In Uzuntarlan's¹⁴ study, it was seen that the cases diagnosed with brain death were mostly hospitalized in the anesthesia and reanimation intensive care unit while in the study of Avcı et al.¹⁵ it was seen that the cases were hospitalized in the brain and neurosurgery intensive care unit. In our study, it was observed that the cases diagnosed with brain death were mostly hospitalized in the anesthesia and reanimation intensive care unit and the neurosurgery intensive care unit in equal numbers. It is thought that the number of brain death detections may vary from service to service, depending on the internal functioning of the hospital and the sensitivity of the healthcare personnel on the issue.

The use of auxiliary tests, or which auxiliary test to use, varies depending on the laws of the country and the facilities of the hospitals.¹⁶ While the use of supportive tests in Spain is around 95%¹¹, the use of supportive tests in two studies conducted in our country was 58.1% and 62%.^{7,17} In our study, the use of supportive tests was 97%, which is higher than other studies conducted in our country. In the study by Sipahioğlu et al.¹⁸ in 1998 examining brain death cases, the most commonly used supportive test was computed tomography angiography with a rate of 30.2%. In our study, digital subtraction angiography was used most frequently as a supporting test, with 70%. We think that the choice of supporting test may be related to hospital conditions and access opportunities.

While organ donation in brain death cases was 70% in a study conducted in Spain, organ donation rates in studies conducted in our country were reported between 19% and 69%.^{7,11,19} In our study, the organ donation rate in brain death cases was 12.1%, which was lower than similar studies in the country. We think that the reasons for this may be that 5 of the cases were not citizens of the Republic of Turkey and were excluded from evaluation for donation and that the organ donation rate may vary by region.

In studies conducted in our country, the mean time from admission to intensive care until the diagnosis of brain death was found to be 2.5-6 days.^{17,18} In our study, similar to the literature, the mean time from admission to intensive care until the diagnosis of brain death was found to be 6.6 days. The mean time from suspicion of brain death to diagnosis of brain death was found to be 1 day in the study conducted by Akbaş et al.¹³ and 3 days in the study conducted by Karasu et al.¹⁰ In our study, this period was also found to be 2 days. In our study, the

mean time from diagnosis of brain death to cardiac arrest in non-donor cases (n=30) was 32.67±24.25 hours, and this time was similar to the study by Karasu et al.¹⁰ and Kuşcu et al.⁷

In our study, we found that age, hypertension, Rh-negative blood group, and the time from hospitalization to brain death diagnosis with intracranial hemorrhage diagnosis were statistically related. We think that this may be due to the fact that the majority of cases were patients with intracranial hemorrhage, hypertension being a major factor in the etiology of patients with spontaneous intracranial hemorrhage, and the poor prognosis of this disease in neurological terms.

In our study, we found that the time from follow-up to diagnosis of brain death was statistically significantly shorter in cases diagnosed in the anesthesia intensive care unit. We think that the time from suspicion of brain death to diagnosis is shorter in anesthesia intensive care units because the brain death detection team in our country includes an anesthesia specialist or intensive care specialist, and they have the competence of brain death detection and care as their specialty.

We found that the time between the diagnosis of brain death and cardiac arrest was statistically significantly shorter in patients with coronary artery disease and in patients diagnosed in the cardiovascular surgery intensive care unit. In their study evaluating the frequency of mortality and risk factors in the intensive care unit, Çakır et al.²⁰ found the highest mortality rate (47.8%) in patients hospitalized due to cardiovascular disease. For this reason, we think that the time from diagnosis to cardiac arrest is shorter in patients with cardiovascular disease.

Limitations

The limitations of the study can be stated as being the study was conducted in a single center with a small number of cases and the retrospective acquisition of the data.

CONCLUSION

It is very important to diagnose brain death in order to increase the number of organ transplants from cadavers. It should be kept in mind that brain death may occur in patients with poor neurological prognosis who are hospitalized with diagnoses such as intracranial hemorrhage and cerebral infarction. In patients who may be potential donors, brain death should be determined quickly, rapid action should be taken after diagnosis, and unnecessary loss of time should be avoided.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Scientific Researches Evaluation and Ethics Committee of Gaziantep City Hospital (Date: 16.10.2024, Decision No: 62/2024).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Arsava EM, Demirkaya S, Dora B, et al. Türk nöroloji derneği beyin ölümü tanı kılavuzu. *Türk Nöroloji Derg.* 2014;20(3):101-104.
2. Mollaret P, Goulon M. Le coma dépassé. *Rev Neurol.* 1959;101:3-15.
3. Alderete JF, Jeri FR, Richardson EP Jr, Sament S, Schwab RS, Young RR. Irreversible coma: a clinical, electroencephalographic and neuropathological study. *Trans Am Neurol Assoc.* 1968;93:16-20.
4. Organ ve doku alınması, saklanması, aşılanması ve nakli hakkında kanun. Kanun numarası 6514 Resmi Gazete 18.01.2014-28886. <https://www.resmigazete.gov.tr/eskiler/2014/01/20140118-1.htm>. Erişim tarihi 30Eylül 2024.
5. <https://www.uptodate.com/contents/diagnosis-of-brain-death> Erişim tarihi: 30Eylül 2024.
6. Palabıyık O. Beyin ölümü tanısı alan hastaların retrospektif analizi. *Online Turkish J Health Sci.* 2020;5(4):631-640. doi:10.26453/otjhs.806855
7. Kuşçu ÖÖ, Aktay M. Beyin ölümü olgularının retrospektif değerlendirilmesi. *Anest Derg.* 2021;29(2):99-104. doi:10.5222/jarss.2021.02997
8. Seifi A, Lacci JV, Godoy DA. Incidence of brain death in the United States. *Clin Neurol Neurosurg.* 2020;195:105885. doi:10.1016/j.clineuro.2020.105885
9. Eira CSLD, Barros MIT, Albuquerque AMP. Organ donation: the reality of an intensive care unit in Portugal. Doação de órgãos: a realidade de uma unidade de cuidados intensivos portuguesa. *Rev Bras Ter Intensiva.* 2018;30(2):201-207. doi:10.5935/0103-507X.20180040
10. Karasu D, Yılmaz C, Karaduman İ, Pekel NB. Beyin ölümü olgularının retrospektif analizi. *J Crit Intensive Care.* 2015;6(2):23. doi:10.5152/dcbbyd.2015.595
11. Escudero D, Valentin M O, Escalante JL, et al. Intensive care practices in brain death diagnosis and organ donation. *Anaesthesia.* 2015;70(10):1130-1139. doi:10.1111/anae.13065
12. Karan E, Elgin E, Ofaz R, et al. Bir Üniversite Hastanesi'nde beyin ölümü tanısı konan olgularda organ bağı oranlarının retrospektif analizi. *Uludağ Üni. Tıp Fak Derg.* 2019;45(1):41-46. doi:10.32708/uutfd.461923
13. Akbaş T, Kurtpınar Z, Şenadım S, et al. Nöroloji yoğun bakım ünitesinde beyin ölümü tanısı konulan olguların incelenmesi. *ACU Sağlık Bil Derg.* 2018;9(3):309-313. doi:10.31067/0.2018.30
14. Uzuntarla Y. Retrospective investigation of brain death and organ donation cases in a training and research hospital. *GKDA Derg.* 2019;25(4):264-269. doi:10.5222/GKDAD.2019.98159
15. Avcı O, Gündoğdu O. Retrospective analysis of the patients with brain death diagnosis in the last five years in our hospital. *Cumhuriyet Med J.* 2019;41(2):385-391. doi:10.7197/223.vi.574315
16. Citerio G, Murphy PG. Brain death: the European perspective. *Semin Neurol.* 2015;35(2):139-144. doi:10.1055/s-0035-1547533
17. Sahin M, Altınay M, Cinar AS, Yavuz H. Retrospective analysis of patients diagnosed with brain death in our hospital in the last 15 years. *Sisli Etfal Hastan Tip Bul.* 2023;57(4):526-530. doi:10.14744/SEMB.2023.65928
18. Sipahioglu H, Elay G, Bingol N, Bahar I. Retrospective analysis of 1998 patients diagnosed with brain death between 2011 and 2019 in Turkey. *J Neuroanaesthesiol Crit Care.* 2022;9(2):106-111. doi:10.1055/s-0042-1750093
19. Kıraklı C, Uçar ZZ, Anıl AB, Özbek İ. The effect of shortening confirmed brain death diagnosis time on organ donation rates in the intensive care unit. *Yoğun Bakım Derg.* 2011;1:8-11. doi:10.5152/dcbbyd.2011.02
20. Çakır E, Kocabeyoğlu GM, Gürbüz Ö, BÖ Sevil, Mutlu NM, Işıl ÖT. Yoğun bakım ünitesinde mortalite sıklığı ve risk faktörlerinin değerlendirilmesi. *Ankara Eği Arş Hast Derg.* 2020;53(1):20-24. doi:10.20492/aeahtd.537879

Traditional and complementary medicine practices in postoperative analgesia

 Münire Babayiğit¹,  Mustafa Alparslan Babayiğit²,  Berrin Koşar¹

¹Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

²Public Health Specialist, Occupational Physician, Ankara, Türkiye

Cite this article: Babayiğit M, Babayiğit MA, Koşar B. Traditional and complementary medicine practices in postoperative analgesia. *Eur J Anesthesiol Intens Care.* 2025;2(1):29-34.

Corresponding Author: Münire Babayiğit, mnroksuz@hotmail.com

Received: 17/11/2024

Accepted: 30/12/2024

Published: 03/02/2025

ABSTRACT

Pharmacological methods are fast-acting, easily applicable and accessible methods with scientifically proven efficacy and standardized protocols. For this reason, it is the most preferred treatment method in the treatment of pain caused by various reasons. However, uncontrolled use of analgesics can sometimes cause more harm than benefit. Sometimes, the use of pharmacologic methods may be limited due to the patient's comorbidities and physiologic limitations, and may not provide the intended level of pain management. Due to the cost, it brings a serious burden to both the individual and the national economy. An individual approach should be the basis of pain management and it would be appropriate to consider the use of traditional and complementary treatment (T&CM) methods in the search for different methods.

Keywords: Postoperative pain, complementary therapies, traditional therapies, analgesia

INTRODUCTION

The World Health Organization defines traditional and complementary therapies (T&CM) as a set of knowledge, skills and practices based on theories, beliefs and experience specific to different cultures, which can be explained or not, used in the prevention of diseases, maintenance of health and well-being, and treatment of diseases.¹ These practices can be used in addition to modern medical practices or as an alternative treatment in cases where they are risky due to the patient's clinical condition.

The training and application area of T&CM practices, which have become widespread in our country as well as all over the world, was regulated by the regulation issued by the Ministry of Health in 2014. In the Official Gazette No. 9158, 15 methods and practices (acupuncture, apitherapy, phytotherapy, hypnosis, leech application, homeopathy, chiropractic, cupping, larva application, mesotherapy, prolotherapy, osteopathy, ozone application, reflexology and music) were accepted as traditional and complementary medicine practices.²

T&CM applications can be applied for different medical indications such as depression, anxiety, menstrual irregularities, diabetes mellitus, hypertension, injury, infection, respiratory problems.^{3,4} Anesthesiologists use different T&CM methods for preoperative anxiolysis, perioperative sedation, postoperative

recovery, analgesia and anti-emesis in the perioperative process.⁵⁻⁷ These methods can be used alone or in combination with modern medical applications depending on the patient's condition. In postoperative analgesia, multimodal analgesia protocols are used to provide effective analgesia and to reduce the side effects of medications. With the addition of T&CM applications to medical treatment protocols, it is expected that possible drug interactions and complications will be further reduced.⁸⁻¹⁰ In this review, T&CM methods that can be used in postoperative analgesia are presented in the light of current literature.

ACUPUNCTURE

Acupuncture is a treatment method that has been practiced for thousands of years. According to the teaching of acupuncture, life energy (QI) flows through 12 main and 8 secondary meridians in the human body. It is accepted that pathology develops when there is any blockage in this energy flow, and health is maintained by reorganizing the energy flow by stimulating the acupuncture points on these meridians.¹¹ The mechanism of action of acupuncture has not been clearly demonstrated. However, in studies in which the effects of stimulation of these points were examined with functional

MRI imaging methods, an increase in activity in brain sections associated with the described effects was found.^{12,13} Specific proresolution mediators (SPMs) such as resolvins, protectins, maresins and lipoxins are lipid molecules produced during the resolution phase of inflammation. Animal experiments suggest that these mediators inhibit inflammatory pain, postoperative pain, neuropathic pain and cancer pain through immune, glial and neuronal modulations. Ear acupuncture has been shown to increase the level of resolvin in guinea pigs and it has been reported that acupuncture may be a guide in explaining the mechanism of analgesia.¹⁴⁻¹⁶

Acupuncture can be used for acute and chronic pain. It is also an effective treatment for postoperative analgesia.¹⁷ Total knee replacement (TKP) is associated with severe postoperative pain. A meta-analysis of twenty RCTs involving 1295 participants investigating the use of acupuncture using transcutaneous electrical acupoint stimulation (TEAS) for analgesia after TKP was performed.¹⁸ TEAS was found to improve several outcomes compared to control groups. Significant reductions in pain were found in the TEAS group at 6 hours, 12 hours, 2, 3, 4, 7 and 14 days postoperatively. In addition, postoperative range of motion (ROM) improved significantly in patients who underwent TEAS. Patients who underwent TEAS experienced fewer analgesic-related side effects and exhibited lower levels of IL-6 and CRP. As a result of the meta-analysis, it was concluded that TEAS application is effective in postoperative analgesia, contributes to functional recovery and is associated with fewer side effects associated with analgesics in patients undergoing TKA.¹⁸

An analysis of 7 studies involving 891 patients on the use of acupuncture after knee replacement showed that acupuncture is an effective analgesic method. In this meta-analysis, Xuehai (SP10), Liangqiu (ST34), Dubi (ST35), Neixiyan (EX-LE4), Yanglingquan (GB34), and Zusanli (ST36) were the most commonly used acupuncture points for analgesia in knee replacement.¹⁹ A large-scale meta-analysis of 41 studies involving 3003 patients in TKP surgery, including the use of different acupuncture methods such as ear, body and transcutaneous electrical stimulation, showed that acupuncture was the most effective method to be used in addition to multimodal analgesia.²⁰

In a meta-analysis examining the efficacy of acupuncture for postoperative analgesia in lumbar disc herniation surgery (LDH), 10 clinical trials involving a total of 838 patients were analyzed. Postoperative VAS scores were lower in the acupuncture groups, and the incidence of side effects was lower than with medication. Acupuncture has been reported to be a safe and effective method of analgesia after LDH operations.²¹

A meta-analysis of 17 studies investigating the use of transcutaneous acupoint electrical stimulation for postoperative analgesia was performed. As a result of this meta-analysis, it was shown that the use of TEAS was effective in the treatment of pain, decreased the frequency of drug-induced dizziness, nausea and vomiting, and its use was recommended as part of multimodal analgesia.²²

In cases where drug use is risky, such as pregnancy and breastfeeding period, the use of acupuncture provides effective analgesia in the mother and protects the mother and baby from drug-related side effects.²³ In a study, the effectiveness of acupuncture use in patients undergoing cesarean section under spinal anesthesia was investigated. It was found that

acupuncture provided effective analgesia compared to standard care, mothers were mobilized early, urinary catheter was removed early, and less nausea and vomiting were observed.²⁴

Acupuncture can be used safely in children as well as adults. In a study investigating the effectiveness of acupuncture after adenotonsillectomy in pediatric patients, LI 4, LI 10, LI 14, LI 20, DU 20, CV 23, Yin Tang points were used. As a result of the study, acupuncture was recommended as an effective, easy to apply and cost-effective treatment method in pediatric patients.²⁵

In a meta-analysis of clinical studies investigating the effect of acupuncture in postoperative analgesia, a significant decrease in postoperative VAS values was observed with acupuncture applications. However, side effects such as nausea, vomiting, dizziness, pruritus and urinary retention due to opioid use have been found to be less common.²⁶ Acupuncture has been recommended to be considered in treatment protocols for postoperative pain management.

PHYTOTHERAPY

Phytotherapy is the systemic or local use of plants in various pharmaceutical forms to protect and treat health. The use of essential oils of plants is called aromatherapy. It can be used in the treatment of preoperative anxiety, postoperative pain, nausea and vomiting in the perioperative process. Echinacea, ephedra, garlic, ginkgo, ginseng, kava, St. John's wort, lavender, St. John's wort, lavender and valerian are commonly used, and lavender essential oil is particularly preferred for analgesia.²⁷

Lavender is a plant with sedative and analgesic activity. In one study, the efficacy of lavender essential oil in analgesia after inguinal hernia operation was investigated. Immediately after surgery, patients inhaled lavender aromatic oil for 20 minutes with mask oxygen. In the pain controls performed in the first 24 hours, VAS values were statistically significantly lower in the aromatherapy group compared to the control group.²⁸ In a randomized, controlled study investigating the efficacy of lavender essential oil in the treatment of pain after gynecological surgery, the control group received only routine analgesic treatment, the placebo group received hand massage with ultrasound gel in addition to routine treatment, and the study group received massage with lavender oil and the pain levels of the patients were followed up afterwards. The pain levels of the patients in the group massaged with lavender oil were found to be statistically significantly lower. As a result of the study, it was stated that massage with lavender essential oil is an effective complementary medicine practice that can be easily applied by nurses in the treatment of postoperative acute pain.²⁹

Lower extremity orthopedic operations are operations in which severe postoperative pain is expected. A randomized, controlled study was conducted to investigate the effectiveness of aromatherapy in the treatment of pain after such operations. In this study, sweet almond oil was used in the control group and citrus oil (*Citrus aurantium*) in the research group. The pain levels of the patients were questioned at 4, 8 and 12 hours after surgery and aromatherapy was applied to patients with a VAS value greater than 3. Pain levels were re-evaluated after aromatherapy. In the study group in which citrus essential oil was used after aromatherapy, there was a statistically significant decrease in pain levels at 4 and 12 hours.³⁰ It has been reported

that aromatherapy with essential oils may be helpful in the treatment of pain after orthopedic surgery.

In obese patients, opioids should be used with caution due to the risk of obesity-related respiratory complications, and multimodal analgesia should be preferred.⁶ In a study, it was found that aromatherapy with lavender essential oil for analgesia in PACU after laparoscopic bariatric surgery significantly reduced opioid use in these patients. As a result of the study, it was stated that aromatherapy may be preferred as a part of multimodal analgesia in the treatment of pain after bariatric surgery.³¹

MUSIC THERAPY

Music therapy is a specialty that uses music and musical activities to meet the physical, psychological, social and mental needs of individuals. It can be used in the treatment of postoperative pain in the perioperative period.³²

The effectiveness of music therapy in the treatment of pain after cesarean section under general anesthesia was investigated. The study group was allowed to listen to music in the style that the patients liked, while the control group received standard treatment. Postoperative PCA was started in both groups and tramadol consumption was compared. It was observed that tramadol consumption was significantly lower in the music therapy group.³³

In an interesting study, music therapy was applied in patients under general anesthesia in laparoscopic gynecological surgeries. Following induction of general anesthesia, the patients were played music with headphones. Routine anesthesia care was applied to the control group. In the postoperative period, VAS values were lower and quality of recovery score (QoR-40) was higher in the group that received music therapy.³⁴

Patients who underwent heart valve replacement were compared with patients who were listened to music for 15 minutes 3 times a day in the postoperative period and patients who received routine standard care. It was determined that the pain and anxiety levels of the patients in the music therapy group were lower. While there was no difference between the diastolic blood pressures of the patients, systolic blood pressure and respiratory rate were found to be lower in the music therapy group. Music therapy seems to have a positive effect on the hemodynamic parameters of patients with anxiolytic and analgesic effects.³⁵

A meta-analysis of 92 clinical studies involving 7385 patients showed that music therapy reduced anxiety and pain sensation in the perioperative period. In the meta-analysis, which emphasized the possibility of bias in the studies, it was reported that age, gender, selected music and anesthesia type had an effect on the result.³²

REFLEXOLOGY

Reflexology is defined as a treatment practice that is applied with special techniques to special reflex points on the hands, feet and ears that are connected to the organs and helps regulate body functions. Each organ in the body represents a specific point on the hands, feet and ears. Since the points on the feet where the organs are reflected are in a larger area, these points are more prominent than the points on the hands and

ears. In reflexology, if pressure is applied to the relevant point, the peripheral nervous system is stimulated. With this stimulus transmitted to the central nervous system, the functioning of the relevant body part is regulated. In addition, a serious anxiolysis is provided in the person with the massage applied to the foot (Figure).³⁶



Figure. Foot reflexology chart

In a randomized controlled study, Öztürk et al.³⁷ investigated the effect of foot reflexology on anxiety and pain after abdominal hysterectomy. Postoperative anxiety level was evaluated by STAI score and pain level by VAS scoring. STAI and VAS scores were lower in the reflexology group compared to the control group in which routine standard postoperative care was provided.

In a study examining the anxiolytic and analgesic effect of ear acupuncture and foot reflexology after cesarean section, it was found that reflexology had anxiolytic and analgesic effect compared to the control group, but acupuncture was much more effective. It has been emphasized that both methods are noninvasive, effective complementary medicine methods that can be used in the treatment of postoperative pain after cesarean section.³⁸

Elmowafy et al.³⁹ compared the group that received standard postoperative care after abdominal surgery with the group that received reflexology in addition to this care in their study on 200 patients. Pain scores were lower and comfort scores were higher in the reflexology group.

OZONE THERAPY

Ozone is a gas consisting of 3 oxygen atoms. Its use in the medical field has been increasing rapidly since World War I.⁴⁰ Its use in ischemia reperfusion injury, cancer, osteoarthritis and sepsis is becoming widespread.

In lumbar disc herniation, it has been reported that ozone treatment alone provides improvement and analgesia equivalent to ozone treatment with betamethasone.⁴⁰

Uslu et al.⁴¹ investigated the use of ozone in gingivectomy and gingivoplasty. The quality of life of the control group, photobiomodulation therapy (PBM) group and ozone therapy group were evaluated with the Oral Health Impact Profile (OHIP-14) questionnaire and pain levels were evaluated with VAS. As a result, the VAS values of the PBM group and the ozone therapy group were found to be lower and it was stated

that these treatments positively affected the quality of life of the patients. A meta-analysis of clinical studies on the application of ozone therapy after impacted mandibular third-molar surgery was performed. As a result of the meta-analysis, it was found that facial swelling and trismus did not decrease in patients treated with ozone therapy, but postoperative pain and analgesic need were less and quality of life was higher. Studies investigating the effectiveness of ozone therapy in reducing postoperative complications were recommended.⁴²

Teixeira et al.⁴³ formed 3 groups for the treatment of pain after ovariectomy in animal experiment. One group received 0.2 mg/kg im meloxicam, one group received rectal ozone and one group received ozone via insulin injector at the acupuncture points LI 4, LIV 3, ST 36, GB 34, SP 6. As a result, both ozone groups achieved analgesia equivalent to the use of nonsteroidal anti-inflammatory drugs. As a result of the study, in which there were no complications related to ozone therapy, it was suggested that ozone therapy may be an alternative analgesic treatment.⁴³

CUPPING THERAPY

Cupping therapy is one of the most commonly used T&CM methods. It is frequently used especially for muscular pain. In the postoperative period, it regulates blood circulation, resolves muscle spasm, reduces inflammation and pain and accelerates the healing process.

Studies have shown that it provides general well-being and improves sleep quality in chronic fatigue syndrome.⁴⁴ It is thought that cupping therapy can be used as a support for this purpose in the postoperative period. In cupping therapy, as in acupuncture and reflexology, it is recommended to apply to certain points according to the indication. However, in a study by Silva et al.⁴⁵ L1-L5 bilateral dry cupping application was compared with sham application in nonspecific chronic low back pain. The results of the study showed that cupping was not superior to sham application. This may be due to the mechanism of action of cupping mainly by regulating local blood circulation. Therefore, local stimulation occurs in both applications.⁴⁵

PROLOTHERAPY

Prolotherapy is a treatment method that stimulates inflammation and regeneration by injecting 5% dextrose into tendons and ligaments. Joint stabilization and analgesia are aimed by strengthening the periarticular ligaments.

In osteoarthritis, prolotherapy is recommended primarily in the preoperative period and in early stage arthrosis. However, prolotherapy has also been shown to be effective in persistent pain that does not go away in the postoperative period.⁴⁶

In an article, the results of prolotherapy applications to 79 patients who complained of long-term pain in the postoperative period due to failed back surgery syndrome (FBSS) are presented. Patients' pain levels were assessed by VAS score, disability status by Oswestry disability index (ODI) and patient satisfaction by 5-point Likert scale. VAS scores and ODI indices of patients were found to decrease significantly after treatment.⁴⁷

MESOTHERAPY AND NEURAL THERAPY

These methods provide analgesia with the use of very low doses of local anesthetics. Injections are made into the surgical area, the surrounding area and the areas corresponding to the relevant dermatome.

In a case report in the literature, a 54-year-old woman presented with a complaint of persistent pain in the incision line after previous surgery. Despite the use of meloxicam, paracetamol and pregabalin, analgesia was not achieved.⁴⁸

Egli et al.⁴⁹ In one of their articles, they shared the results of their neural therapy applications to 280 patients with resistant chronic pain. In 60 patients, it was reported that the pain level did not change, 52 patients developed mild, 126 patients developed significant improvement, while 41 patients were completely pain-free. It was emphasized that patients should be given the chance of neural therapy instead of long-term, long-acting and costly treatments.⁴⁹

Randomized, controlled studies on the use of mesotherapy and neural therapy in the postoperative period are needed.

HIRUDOTHERAPY

The leeches used in medical treatments in our country are *H. verbana* and *H. Sulukii* species. Leeches provide analgesic and anti-inflammatory effects by secreting substances such as antistasin, hirustasin, ghilantens, leech-derived tryptase inhibitor, complement C1 inhibitor.

In a study examining the use of hirudotherapy in various chronic pain conditions including osteoarthritis, an analgesic effect lasting up to 12 months after hirudotherapy was reported.⁵⁰

A meta-analysis analyzed 15 clinical trials. As a result of the meta-analysis, it was reported that leech therapy may provide analgesic effect in different patients. It is recommended to use the appropriate leech species and the correct treatment protocol.⁵¹

In addition to providing analgesia in the postoperative period, leeches can also be used due to their edema reducing and blood circulation regulating effects.⁵²

MUSIC THERAPY

A study was conducted to examine the effect of music on the recovery process after knee replacement surgery. There was no statistically significant difference in anxiety scores between the two groups. However, the pain score at the 60th postoperative minute in the music therapy group was significantly lower than in the control group.⁵³ Akelma et al.⁵⁴ investigated the effects of preoperative music therapy on anxiety and recovery in 255 patients scheduled for inguinal hernia surgery under general anesthesia. In this study, patients were divided into 3 groups. One group was the control group and standard anesthesia management was performed. In the second group, patients listened to classical music, while in the third group, patients listened to the music they wanted. As a result of the study, it was observed that the anxiety scores of the patients in the third group decreased significantly. However, there was no statistically significant difference between the pain scores.⁵⁴

Music is a safe and cost-effective intervention, but more clinical studies are needed to investigate its effectiveness in postoperative pain.

CONCLUSION

This review demonstrates the applicability of different traditional and complementary medicine practices in postoperative analgesia. When the literature is reviewed, it is seen that acupuncture, music therapy and phytotherapy are used relatively more commonly. Although these methods can be used alone, it is stated in the articles that they are preferred as part of multimodal analgesia. Protecting patients from possible side effects, providing effective analgesia and increasing patient satisfaction are essential in health care.

However, more randomized controlled studies are needed to investigate the effectiveness of these treatment methods in different types of surgeries and different patient groups.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

- WHO traditional medicine strategy 2014-2023. WHO Library Cataloguing-in publication Data.
- TC Resmi Gazete (2014) Geleneksel ve tamamlayıcı tıp uygulamaları yönetmeliği. 27 Ekim 2014. Sayı: 29158. Başbakanlık Basımevi. Ankara
- Mutlu NM, Balkız Soysal Ö, Titiz AP, Zengin EN, Akçaboy ZN. Acupuncture for critically ill patients. *Eurasian J Anesthesiol Intens Care*. 2024;1(2):35-41. doi:10.51271/EAJAIC-0008
- Wang JX, Sun R, Si DX, et al. Clinical practice guidelines of Chinese patent medicine in China: a critical review. *Complement Ther Med*. 2024;85: 103077. doi:10.1016/j.ctim.2024.103077
- Babayigit M, Babayigit MA, Honca M, Koşar B, Özayar E. Knowledge, attitude and behaviors on traditional and complementary medicine practices among our patients with chronic pain complaints. *J Tradit Complem Med*. 2021;4(2):210-218. doi:10.5336/jtracom.2020-80884
- Honca M, Honca T, Babayigit M, Bulus H. The impact of acupuncture on postoperative nausea and vomiting in obese adult patients undergoing laparoscopic sleeve gastrectomy: a randomized controlled trial. *J Laparoendosc Adv Surg Tech A*. 2022;32(7):775-780. doi:10.1089/lap.2021.0406
- Babayigit M, Babayigit MA. Traditional and complementary medicine applications in preoperative anxiety. *Eur J Anesthesiol Intensive Care*. 2024; 1(1):16-19. doi:10.51271/EAJAIC-0004
- Zimpel SA, Torloni MR, Porfirio GJ, Flumignan RL, da Silva EM. Complementary and alternative therapies for post-caesarean pain. *Cochrane Database Syst Rev*. 2020;9(9):CD011216. doi:10.1002/14651858.CD011216. pub2
- Levy I, Attias S, Cohen L, et al. Postoperative analgesia by adding acupuncture to conventional therapy, a non-randomized controlled trial. *J Complement Integr Med*. 2018;16(2):20180028. doi:10.1515/jcim-2018-0028
- Liu N, Liu G, Chang X, et al. Combining various acupuncture therapies with multimodal analgesia to enhance postoperative pain management following total knee arthroplasty: a network meta-analysis of randomized controlled trials. *Front Neurol*. 2024;15:1361037. doi:10.3389/fneur.2024.1361037
- Chae Y, Olausson H. The role of touch in acupuncture treatment. *Acupunct Med*. 2017;35(2):148-152. doi:10.1136/acupmed-2016-011178
- Bai L, Yan H, Li L, et al. Neural specificity of acupuncture stimulation at pericardium 6: evidence from an fMRI study. *J Magn Reson Imaging*. 2010; 31(1):71-77. doi:10.1002/jmri.22006
- Takamoto K, Urakawa S, Sakai K, Ono T, Nishijo H. Effects of acupuncture needling with specific sensation on cerebral hemodynamics and autonomic nervous activity in humans. *Int Rev Neurobiol*. 2013;111:25-48. doi:10.1016/B978-0-12-411545-3.00002-X
- Tao X, Lee MS, Donnelly CR, Ji RR. Neuromodulation, specialized proresolving mediators, and resolution of pain. *Neurotherapeutics*. 2020; 17(3):886-899. doi:10.1007/s13311-020-00892-9
- Fang JF, Du JY, Shao XM, Fang JQ, Liu Z. Effect of Electroacupuncture on the NTS is modulated primarily by acupuncture point selection and stimulation frequency in normal rats. *BMC Complement Altern Med*. 2017; 17(1):182. doi:10.1186/s12906-017-1690-7
- Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci*. 2003;26(1):17-22. doi:10.1016/s0166-2236(02)00006-1
- Janssens LA, Rogers PA, Schoen AM. Acupuncture analgesia: a review. *Vet Rec*. 1988;122(15):355-358. doi:10.1136/vr.122.15.355
- Zhang L, Zhang Z, Chen Z, et al. Transcutaneous electrical acupoint stimulation for rehabilitation after total knee arthroplasty: a systematic review and meta-analysis. *Am J Transl Res*. 2024;16(5):1484-1498. doi:10.62347/VZLG2317
- Ko HF, Chen CH, Dong KR, Wu HC. Effects of acupuncture on postoperative pain after total knee replacement: systematic literature review and meta-analysis. *Pain Med*. 2021;22(9):2117-2127. doi:10.1093/pm/pnab201
- Liu N, Liu G, Chang X, et al. Combining various acupuncture therapies with multimodal analgesia to enhance postoperative pain management following total knee arthroplasty: a network meta-analysis of randomized controlled trials. *Front Neurol*. 2024;15:1361037. doi:10.3389/fneur.2024.1361037
- Zhang W, Liu H, Le X, et al. Acupuncture for postoperative pain of lumbar disc herniation: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2022;101(49):e32016. doi:10.1097/MD.00000000000032016
- Wang D, Shi H, Yang Z, et al. Efficacy and safety of transcutaneous electrical acupoint stimulation for postoperative pain: a meta-analysis of randomized controlled trials. *Pain Res Manag*. 2022;2022:7570533. doi:10.1155/2022/7570533
- Usichenko TI. Acupuncture as part of multimodal analgesia after caesarean section. *Acupunct Med*. 2014;32(3):297-298. doi:10.1136/acupmed-2014-010584
- Usichenko TI, Henkel BJ, Klausenitz C, et al. Effectiveness of acupuncture for pain control after cesarean delivery: a randomized clinical trial [published correction appears in JAMA Netw Open. 2022;5(4):e229622]. *JAMA Netw Open*. 2022;5(2):e220517. doi:10.1001/jamanetworkopen.2022.9622
- Ochi JW. Acupuncture instead of codeine for tonsillectomy pain in children. *Int J Pediatr Otorhinolaryngol*. 2013;77(12):2058-2062. doi:10.1016/j.ijporl.2013.10.008
- Sun Y, Gan TJ, Dubose JW, Habib AS. Acupuncture and related techniques for postoperative pain: a systematic review of randomized controlled trials. *Br J Anaesth*. 2008;101(2):151-160. doi:10.1093/bja/aen146
- Ang-Lee MK, Moss J, Yuan CS. Herbal medicines and perioperative care. *JAMA*. 2001;286(2):208-216. doi:10.1001/jama.286.2.208
- Bagheri H, Salmani T, Nourian J, et al. The effects of inhalation aromatherapy using lavender essential oil on postoperative pain of Inguinal hernia: a randomized controlled trial. *J Perianesth Nurs*. 2020;35(6):642-648. doi:10.1016/j.jopan.2020.03.003
- Mizrak Sahin B, Culha I, Gursoy E, Yalcin OT. Effect of massage with lavender oil on postoperative pain level of patients who underwent gynecologic surgery: a randomized, placebo-controlled study. *Holist Nurs Pract*. 2021;35(4):221-229. doi:10.1097/HNP.0000000000000400
- Bargi S, Bahraminejad N, Jafari S, Fallah R. The effect of aromatherapy with Citrus aurantium aroma on pain after orthopedic surgery: a randomized clinical trial. *J Caring Sci*. 2023;12(2):116-122. doi:10.34172/jcs.2023.30120
- Kim JT, Ren CJ, Fielding GA, et al. Treatment with lavender aromatherapy in the post-anesthesia care unit reduces opioid requirements of morbidly obese patients undergoing laparoscopic adjustable gastric banding. *Obes Surg*. 2007;17(7):920-925. doi:10.1007/s11695-007-9170-7

32. Köhlmann AYR, de Rooij A, Kroese LF, van Dijk M, Hunink MGM, Jeekel J. Meta-analysis evaluating music interventions for anxiety and pain in surgery. *Br J Surg*. 2018;105(7):773-783. doi:10.1002/bjs.10853
33. Sen H, Yanarates O, Sızlan A, Kılıç E, Ozkan S, Dağlı G. The efficiency and duration of the analgesic effects of musical therapy on postoperative pain. *Agri*. 2010;22(4):145-150.
34. Choi EK, Baek J, Lee D, Kim DY. Effect on music therapy on quality of recovery and postoperative pain after gynecological laparoscopy. *Medicine (Baltimore)*. 2023;102(9):e33071. doi:10.1097/MD.00000000000033071
35. Dong Y, Zhang L, Chen LW, Luo ZR. Music therapy for pain and anxiety in patients after cardiac valve replacement: a randomized controlled clinical trial. *BMC Cardiovasc Disord*. 2023;23(1):32. doi:10.1186/s12872-023-03058-5
36. Dehghanmehr S, Sargazi GH, Biabani A, Nooraiein S, Allahyar J. Comparing the effect of acupressure and foot reflexology on anxiety and depression in hemodialysis patients: a clinical trial. *Med Surg Nurs J*. 2019;8(4):e100386. doi:10.5812/msnj.100386
37. Öztürk R, Sevil Ü, Sargin A, Yücebilgin MS. The effects of reflexology on anxiety and pain in patients after abdominal hysterectomy: a randomised controlled trial. *Complement Ther Med*. 2018;36:107-112. doi:10.1016/j.ctim.2017.12.005
38. Mousavi FS, Golmakani N, Valiani M, Bahrami Taghanaki HR, Rezaei F. Comparison of two methods of complementary medicine on postoperative pain and anxiety: a randomized clinical trial. *J Edu Health Promot*. 2023;12(1):458. doi:10.4103/jehp.jehp_1246_22
39. Elmowafy AOI, Gaber EMM, Mohamed NAM. Impact of foot reflexology on pain intensity, physiological indicators, and comfort among patients undergoing abdominal surgery. *Egypti J of Health Care*. 2024;15(1):1434-1449. doi:10.21608/ejhc.2024.346544
40. Hao K, Tang S, Xie H, Li X, He X. Application of ozone therapy in interventional medicine. *J Interv Med*. 2019;2(1):8-11. doi:10.1016/j.jimed.2019.05.003
41. Uslu MÖ, Akgül S. Evaluation of the effects of photobiomodulation therapy and ozone applications after gingivectomy and gingivoplasty on postoperative pain and patients' oral health-related quality of life. *Lasers Med Sci*. 2020;35(7):1637-1647. doi:10.1007/s10103-020-03037-8
42. Chaudhry K, Rustagi N, Bali R, et al. Efficacy of adjuvant ozone therapy in reducing postsurgical complications following impacted mandibular third-molar surgery: a systematic review and meta-analysis. *J Am Dent Assoc*. 2021;152(10):842-854.e1. doi:10.1016/j.adaj.2021.05.006
43. Teixeira LR, Luna SP, Taffarel MO, et al. Comparison of intrarectal ozone, ozone administered in acupoints and meloxicam for postoperative analgesia in bitches undergoing ovariohysterectomy. *Vet J*. 2013;197(3):794-799. doi:10.1016/j.tvjl.2013.05.015
44. Meng XD, Guo HR, Zhang QY, et al. The effectiveness of cupping therapy on chronic fatigue syndrome: a single-blind randomized controlled trial. *Complement Ther Clin Pract*. 2020;40:101210. doi:10.1016/j.ctcp.2020.101210
45. Almeida Silva HJ, Barbosa GM, Scattone Silva R, et al. Dry cupping therapy is not superior to sham cupping to improve clinical outcomes in people with non-specific chronic low back pain: a randomised trial. *J Physiother*. 2021;67(2):132-139. doi:10.1016/j.jphys.2021.02.013
46. Barawid EL, Davis SM, Ardestani A, Turchi RD. Periarticular dextrose prolotherapy after total knee arthroplasty: a retrospective case series. *AME Surg J*. 2023;3:28 doi:10.21037/asj-21-38
47. Solmaz İ, Akpınar S, Örsçelik A, et al. Dextrose injections for failed back surgery syndrome: a consecutive case series. *Eur Spine J*. 2019;28(7):1610-1617. doi:10.1007/s00586-019-06011-3
48. Muttalib A, Wirawan NS. Neural prolotherapy in persistent post-surgery pain: a case report. *J Anesthesiol Clin Res*. 2023;4(1):388-391.
49. Egli S, Pfister M, Ludin SM, Puente de la Vega K, Busato A, Fischer L. Long-term results of therapeutic local anesthesia (neural therapy) in 280 referred refractory chronic pain patients. *BMC Complement Altern Med*. 2015;15(1):200. doi:10.1186/s12906-015-0735-z
50. Loeser J, Lauer B, Plata C, Perrar KM, Hucho T, Kulbida R. Hirudotherapy attenuates arthritic pain in patients with various chronic pain syndromes: a retrospective analysis. *J Integr Med*. 2020;18(5):425-433. doi:10.1016/j.joim.2020.07.003
51. Rajfur K, Rajfur J, Fras-Labanc B. Does the use of hirudotherapy reduce pain? A narrative review. *Med Sci Pulse*. 2024;18(2):22-27. doi:10.5604/01.3001.0054.6065
52. Abdullah S, Dar LM, Rashid A, Tewari A. Hirudotherapy/leech therapy: applications and indications in surgery. *Arch Clin Exp Surg*. 2012;1(3):172-180. doi:10.5455/aces.20120402072447
53. Aris A, Sulaiman S, Che Hasan MK. Effects of music therapy on physiological outcomes for post-operative total knee arthroplasty (TKA) patients. *Enferm Clin*. 2021;31(Supl 2):S10-15. doi:10.1016/j.enfcli.2020.10.006
54. Akelma, FK, Altınsoy S, Nalbant B, Özkan D, Ergil J. Comparison of classical and patient-preferred music on anxiety and recovery after inguinal hernia repair: a prospective randomized controlled study. *Perioper Med*. 2024;13(1):89. doi:10.1186/s13741-024-00434-3

Anesthesia for urological procedures

 **Erbil Türksal**

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatoryum Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Cite this article: Türksal E. Anesthesia for urological procedures. *Eur J Anesthesiol Intens Care*. 2025;2(1):35-39.

Corresponding Author: Erbil Türksal, drerbilturksal@hotmail.com

Received: 04/12/2024

Accepted: 10/01/2025

Published: 03/02/2025

ABSTRACT

Urological procedures are performed on patients of varying ages, including pediatric and elderly individuals. Given the high prevalence of renal dysfunction in patients undergoing urological surgery, a comprehensive preoperative assessment is of particular importance, with a particular focus on renal function. There are a number of potential risks associated with patient positioning and position-related management during surgical procedures. It is crucial to consider the potential for complications, such as nerve damage and respiratory changes, when determining the optimal position for each patient, taking into account safety concerns. It is essential to determine the optimal anesthesia technique for urological surgical procedures, to identify potential complications, and to establish invasive monitoring protocols for high-risk cases. A comprehensive approach is essential for ensuring patient safety and attaining optimal surgical outcomes in urological procedures.

Keywords: Urology, anesthesia, management, patient safety

INTRODUCTION

Although the majority of patients who undergo genitourinary surgery procedures are elderly, these surgical procedures are performed on patients of all age groups. With appropriate perioperative anesthesia management; this process can be successfully managed despite its unique challenges, including physiological changes and comorbid conditions in the geriatric population and physiological and congenital problems of the pediatric population.^{1,2}

Renal dysfunction is more common in patients undergoing urologic surgery than in other surgical groups. In the preoperative evaluation, the volume status of the patients, cardiac and pulmonary findings that may develop accordingly, complete blood count, renal function tests (urea, creatinine, glomerular filtration rate, creatinine clearance) and electrolyte values should be meticulously examined. In patients receiving renal replacement therapy, dialysis is generally recommended before surgery and acidemia should be monitored by blood gas analysis. Since the elimination of most of the drugs to be used during anesthesia is renal, it should be taken into consideration that dosage adjustment will be required to prevent accumulation of the drug itself or its metabolite in renal failure.^{2,3}

PATIENT POSITIONS

The patient can be placed in different positions on the operating table according to the type of surgical procedure. While increasing the comfort of the surgical team by giving the appropriate position, the comfort of the patient (especially awake patients under regional anesthesia) should not be ignored. With the given position, minimum changes in respiratory and hemodynamic parameters should be ensured and possible nerve damage should be prevented.⁴

Supine Position

It is the most commonly used position. It is the standard for induction of anesthesia even if the patient will be operated on in another position. The head and neck should be supported with a suitable pillow. The arms should be spread at maximum 90 degrees to protect from brachial plexus nerve injury. In radical surgeries such as cystectomy, retropubic prostatectomy, pelvic lymph node dissection, patients are hyperextended in the supine position to facilitate access to the pelvis.^{4,5}

Lithotomy Position

It is the most used position after the supine position in gynecological and urological procedures. Two staff are required to ensure that both legs can move simultaneously while

positioning. Incorrect positioning and inadequate padding can lead to nerve damage. Most commonly, loss of dorsiflexion of the foot occurs as a result of inadequate support of the lateral thigh and damage to the common peroneal nerve. Inadequate medial thigh support may result in saphenous nerve damage and loss of sensation on the medial aspect of the leg, while excessive thigh flexion may result in obturator/femoral/sciatic nerve damage. It should be remembered that compartment syndrome can develop with prolonged lithotomy. In addition to nerve damage, lithotomy also has adverse respiratory and hemodynamic effects. Functional residual capacity decreases with positioning, so atelectasis and hypoxia may develop. Elevating the legs shifts the vascular volume towards the centre, increasing blood pressure and cardiac output. When the operation is completed and the patient is returned to the supine position, care should be taken to avoid hypotension, as the blood will return to the lower limb in the opposite direction.^{5,6}

Prone Position

In this position, the patient lies face down on the table. During positioning, attention should be paid to malposition of the endotracheal tube and, after turning the patient prone, auscultation should be used to confirm that both lungs are participating in respiration. Special pillows should be used to prevent pressure on the eyes and nose. In order for the chest to expand properly, the chest wall needs to be supported on both sides, particularly by reducing pressure on the woman's breasts. Similarly, the abdominal wall should be supported on both sides to prevent an increase in intra-abdominal pressure, and care should be taken to avoid pressure on the genitals, especially in men. Bone contact areas should be supported with soft padding.^{4,5}

Lateral Decubitus Position

In this position, the patient lies on the right or left side. As endotracheal tube malposition may occur after positioning, the same precautions should be taken as in the prone position. The head and neck should be adequately supported to ensure axial alignment. Brachial plexus damage should be prevented by supporting the underlying axilla. The lower leg should be semiflexed, the thigh extended and supported by a soft material such as a pillow, and the bone contact areas also supported by soft pads. Ventilation/perfusion mismatch develops with position, functional residual capacity in the underlying lung decreases and atelectasis develops. The patient is placed in the lateral decubitus position and hyperextension is applied to facilitate access to the renal pelvis.^{4,7}

Trendelenburg Position

This is the head-down position when the patient is supine. The endotracheal tube may slide deeper during positioning and after positioning it should be confirmed that both lungs are participating in breathing. As a result of gravity, the intra-abdominal organs are directed cephalad, which increases the intrathoracic pressure. Because the patient's head is below the level of the heart, intracranial pressure increases over time and head and neck oedema may occur. Venous drainage of the eye may be impaired and optic nerve damage may occur with increased intracranial pressure. Particular attention should be paid to the possibility of developing oedema of the face, eyes, tongue, larynx and brain due to the extreme degree of trendelenburg position in robotic surgery.^{4,7,8}

ENDOUROLOGICAL INTERVENTIONS

Cystoscopy

It is the most common urological procedure. The lithotomy position is used for the procedure. In children, general anesthesia is used. In adults, the procedure can be performed under general anesthesia, regional anesthesia or local anesthesia, with or without sedation.

If general anesthesia is preferred, LMA is usually sufficient due to the short duration of the procedure. If regional anesthesia is preferred, spinal or epidural anesthesia including the T10 dermatome is sufficient. Due to the shortness of the urethra, topical anesthesia is more commonly used in women.^{3,9,10}

Transurethral Resection of Bladder Tumor (TUR-BT)

The incidence of bladder cancer is three times higher in men than in women. It is the fourth most common type of cancer in men and the ninth most common type of cancer in women. In the TUR-BT procedure, tumor tissue that has formed in the bladder is removed by continuously washing the bladder and applying electric current to a special ring through the cystoscope.³

The procedure can be performed under general anesthesia or regional neuraxial anesthesia. A sensory block involving the T10 dermatome is sufficient for neuraxial anesthesia.^{1,10} If the tumor is located on the lateral wall of the bladder, the obturator nerve will be stimulated with each use of the electrocautery in patients under spinal/epidural anesthesia due to the anatomical proximity of the obturator nerve, and adduction movement will occur in the leg. To prevent this movement, an obturator nerve block should also be performed when spinal/epidural anesthesia is to be used in patients with bladder sidewall tumors.^{11,12}

Transurethral Resection of the Prostate (TUR-P)

It is the most commonly used surgical procedure for the treatment of benign prostatic hyperplasia. Just like in the TUR-BT procedure, continuous washing is done and an electric current is given to the ring passed through the cystoscope and the prostate tissue is resected.

General anesthesia or neuraxial anesthesia may be preferred. Neuraxial anesthesia requires a sensory block at the T10 level.^{3,9}

Some complications may occur due to the characteristics of the prostate tissue and the irrigation fluid used. Bleeding, TURP syndrome, bladder perforation, hypothermia and disseminated intravascular coagulation (DIC) are some of these complications. Perforation of the prostate capsule occurs in 2% of patients and if it does, surgery should be terminated as soon as possible. Although bleeding is common during a prostate resection, it can be easily controlled. However, continuous irrigation causes blood to mix with the irrigation fluids and the amount of blood is not easy to calculate. DIC can occur as a result of thromboplastin released from the prostate tissue during the intraoperative process. Hypothermia occurs when large volumes of irrigation solution are used and not warmed sufficiently. If the patient shivers because they are cold, this can dislodge the clot and cause the bleeding to start again.^{13,14}

TURP syndrome is a multifactorial condition that affects the central nervous system (CNS), cardiovascular system, respiratory system and metabolic homeostasis as a result of

excessive irrigation solution absorption (at least 2 liters). Early clinical symptoms include a burning sensation in the face and neck, anxiety and lethargy. Headache and irritability are other CNS findings. Eventually there can be blurred vision, confusion, seizures and finally coma. CNS findings are due to acute hyponatremia resulting from the absorption of any type of irrigation solution and hyperglycinemia/hyperammonemia when glycine is used as an irrigation solution. The rate and amount of irrigation solution absorbed depends on factors such as the hydrostatic pressure of the solution, bladder distension, the size of the venous sinuses opened by the resection and the length of the resection period. As regional anesthesia is superior to general anesthesia, the operation must be terminated quickly if the patient develops clinical symptoms and TUR syndrome is suspected. Renal function tests, electrolytes, glucose and arterial blood gas sampling should be obtained. Treatment of TUR syndrome should be based on the severity of symptoms. If symptoms are mild, the serum sodium level is greater than 120 mEq/L. In this case, loop diuretics together with fluid restriction are sufficient to correct serum sodium. If the serum sodium level is less than 120 mEq/L, a 3% hypertonic sodium chloride infusion should be administered at a rate of not more than 0.5 mEq/L per hour.^{15,16}

One of the major complications of TUR-P is sepsis. Sepsis is significantly associated with a higher prostate volume and also with a longer duration of the TUR-P, the group of antibiotics used for prophylaxis and a longer duration of catheterisation. On the other hand, the data about antibiotic prophylaxis in TUR-P are controversial and outdated.¹ It may be advisable to send urine cultures from patients undergoing TURP in the preoperative period and to use antibiotics in case of bacterial growth.¹⁷

Ureteroscopy (URS) / Retrograd Intrarenal Surgery (RIRS)

The URS procedure uses a rigid ureteroscope to fragment small and medium-sized ureteral stones, and the RIRS procedure uses a flexible ureteroscope to fragment small and medium-sized kidney stones. Smaller stones are passed in the urine, and larger stones are removed with a basket. A double-J stent is usually placed after the procedure.

While general anesthesia or neuraxial regional anesthesia at the T6 sensory level may be preferred for URS, general anesthesia is generally preferred for RIRS.^{3,10}

PERCUTANEOUS NEPHROLITHOTOMY (PNL)

PNL is performed on kidney stones larger than 2 cm through a 1 cm incision on the patient's back. The stone, the location of which has been determined using fluoroscopy, is reached with a nephroscope through an incision in the back. The broken stone pieces are removed from the body. At the end of the operation, a nephrostomy catheter is placed in the patient.⁹

General anesthesia is preferred. Attention should be paid to the complications of the prone position as patients are operated on in this position. Nowadays, peripheral nerve/plane blocks such as quadratus lumborum block (QLB) and erector spina plane block (ESP) can be applied for postoperative analgesia.^{18,19}

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL)

ESWL is the process of focusing repeated high-energy sound waves on the stone to break up upper ureteral stones. The fragmented stones are passed in the urine.

General anesthesia has advantages such as control of the patient's movements and breathing. In this way, focused high-energy waves can be prevented from damaging tissues such as the lungs and intestines.

High energy shock waves may trigger arrhythmias in patients with a history of arrhythmias or in patients with a pacemaker or ICD. In addition, shock waves can damage the internal components of these devices.²⁰

RADICAL SURGERY

Radical Retropubic Prostatectomy (RRP)

RRP is a surgical procedure used to treat prostate cancer by removing prostate tissue and anastomosing the neck of the bladder directly to the urethra. To prevent postoperative erectile dysfunction, nerve-sparing surgery has become more common.

A combination of general anesthesia and neuraxial techniques is often preferred for postoperative pain management. Excessive hyperextension in the supine or even Trendelenburg position is very difficult for the awake patient to tolerate.²¹ Bleeding is the most important complication that can occur during the intraoperative and postoperative period. However, deep vein thrombosis (DVT), pulmonary thromboembolism (PTE) and air embolism from the prostate tissue above the level of the head are other complications that may be seen. Invasive arterial monitoring and insertion of at least two large peripheral vascular lines or, if necessary, a central venous catheter are recommended for anesthesia management.^{9,22,23}

Radical Cystectomy

The surgical procedure entails the complete removal of all anterior pelvic organs in the treatment of advanced bladder tumors. Following cystectomy, the ureters are connected to a segment of bowel, forming a urinary diversion.

In most cases, general anesthesia and neuraxial regional anesthesia techniques are combined.²⁴ The surgical procedure is typically prolonged and associated with significant blood loss. It is necessary that invasive arterial monitoring is conducted, and that a central venous catheter or at least two peripheral vascular access points with large lumens are established. The administration of hypotensive anesthesia has been demonstrated to result in a reduction in the incidence of bleeding. It is of significant importance to provide appropriate intravenous hydration in order to ensure adequate urine flow following the anastomosis of the ureters. The prolonged contact of urine with the intestinal mucosa, which occurs as a consequence of slow urine flow, has been identified as a potential cause of metabolic disorders. In the event of an ileal ureteral anastomosis, there is a potential for hyperchloremic metabolic acidosis to occur. With a jejunal ureteral anastomosis, the

possibility of hyponatremia, hypochloremia, hyperkalemia, and metabolic acidosis arises. As with RRP, other potential complications include DVT and PTE.^{23,25}

Radical Nephrectomy

Radical nephrectomy is a surgical procedure performed for renal cell carcinoma, the most common type of kidney tumor, which is resistant to chemotherapy and radiation therapy. It is not uncommon for paraneoplastic syndromes, such as hypertension, hypercalcemia and erythrocytosis, to be observed in these patients. In a minority of patients, comprising 5 to 10% of cases, tumor tissue extends as a thrombus into the renal vein and inferior vena cava. In a range of between comprising 5 to 10% of cases, tumor tissue is observed to extend as a thrombus into the renal vein and inferior vena cava.²⁶

It is common practice to utilise both general anesthesia and neuraxial regional anesthesia techniques in conjunction with one another. Given the likelihood of hemorrhage, it is recommended that invasive arterial monitoring be conducted. It is advised that at least two wide-lumen peripheral vascular access or central venous catheters be inserted. The tumor has extended to the right atrium via the inferior vena cava, which renders central venous catheterisation an inherently risky procedure due to the potential for tumor rupture and pulmonary embolisation. Patients are operated on in the lateral decubitus position, which entails hyperextension. It is of the utmost importance to exercise caution with regard to the potential complications associated with this particular position, which have been previously discussed.^{23,26}

Retroperitoneal Lymph Node Dissection

This surgical procedure is performed for the purposes of staging and treatment of nonseminomatous germ cell tumors. A midline incision is employed to facilitate the removal of lymphatic tissue situated between the bifurcation of the iliac vessels and the renal vessels. As a consequence of sympathectomy, the ability to ejaculate is irreversibly lost, resulting in complete infertility in patients who have undergone the procedure.²⁷

Due to the significant postoperative pain typically experienced by patients, general anesthesia is often combined with neuraxial regional anesthesia techniques. Patients who receive chemotherapy with bleomycin in the preoperative period are at risk of developing postoperative oxygen toxicity, volume overload and ARDS. It is not uncommon for atelectasis to occur in patients who have undergone surgery and who have not received adequate postoperative analgesia.²⁸

Radical Orchiectomy

It constitutes the primary treatment for testicular tumors. The procedure may be conducted with the patient under either general or regional anesthesia. It is imperative that the anesthetist exercise caution to avoid reflex bradycardia, which may result from the traction of the spermatic cord.⁹

UROLOGICAL LAPAROSCOPIC / ROBOTIC SURGERY

The advancement of technology has led to a significant expansion in the range of urological laparoscopic procedures, which now encompass nephrectomy, prostatectomy, cystectomy and pyeloplasty.

General anesthesia is the preferred method for patients undergoing laparoscopic surgery. However, if general anesthesia is contraindicated, T4 high-level neuraxial block methods may be employed as an alternative. The Trendelenburg position with pneumoperitoneum also has an adverse effect on respiratory dynamics, particularly in patients with a high body-mass index and during prolonged surgical procedures. The decompression of the stomach with a nasogastric tube and the emptying of the bladder with a Foley catheter are standard procedures in laparoscopic surgery. In the event that invasive arterial monitoring is required, it may be applied.²³

It has been demonstrated that an excessive Trendelenburg position during robotic surgery may result in the development of oedema in various regions of the body, including the face, eyelids, tongue, larynx and brain. This is attributed to the congestion of the venous system. Severe edema of the airways may render extubation of the patient challenging. Furthermore, once the position has been established, it becomes challenging to gain access to the patient in robotic surgery. It is of the utmost importance that the vascular access and arterial cannula are positioned and fixed meticulously.²²

SCROTAL SURGERY

The most common indications for scrotal surgery are hydrocele and varicocele. General anesthesia or neuraxial regional anesthesia techniques may be preferred. It is important to exercise caution in the event of reflex bradycardia, which may occur as a result of traction on the spermatic cord.⁹

PEDIATRIC SURGERY

The most common indications for pediatric urological surgery are circumcision, orchidopexy, hypospadias, epispadias and ureteropelvic stenosis.

The administration of general anesthesia is typically the preferred option. Postoperative pain can be managed with the use of caudal, penile, or local anesthetic applications. The LMA is frequently the preferred choice for short-term surgical procedures.^{29,30}

PAIN CONTROL

The mitigation and therapy of pain is one of the most important primary medical tasks. Some of the urogenital operative procedures only cause little pain (e.g. vesical interventions or operations of the male genitalia). In these cases, oral analgesia using an NSAID and/or weak opioid is usually sufficient. Other more invasive operations, e.g. nephrectomy and cystectomy, result in severe pain and disturbance of gastrointestinal function, requiring intravenous opioid or perispinal therapy. The latter includes intrathecal (spinal) and epidural infusion of local anaesthetics with or without opioids. Nowadays, peripheral nerve/plane blocks such as quadratus lumborum block (QLB) and erector spina plane block (ESP) can be applied for postoperative analgesia. Multimodal analgesia not only enhances patient satisfaction but also improves the surgical outcome.³¹

CONCLUSION

Effective anesthesia management is critical to the success of urological surgical procedures, ensuring both patient safety

and optimal outcomes. This requires a thorough understanding of the unique physiological considerations across various patient populations and procedure-specific requirements. Comprehensive preoperative evaluations, meticulous attention to patient positioning, and tailored anesthetic techniques are fundamental to minimizing complications and enhancing recovery. As technology advances and surgical methods evolve, the role of anesthesia must adapt to address new challenges, particularly in robotic and minimally invasive surgeries. Ultimately, a multidisciplinary approach that integrates anesthesiology, surgical expertise, and postoperative care is essential for improving patient experiences and outcomes in urological surgery.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

- Cousins J, Howard J, Borra P. Principles of anaesthesia in urological surgery. *BJU Int*. 2005;96(2):223-229. doi:10.1111/j.1464-410X.2005.05664.x
- Koo CH, Ryu JH. Anesthetic considerations for urologic surgeries. *Korean J Anesthesiol*. 2020;73(2):92-102. doi:10.4097/kja.19437
- Alaali HH, Irwin MG. Anaesthesia for urological surgery. *Anaesthesia Int Care Med*. 2021;22(7):449-453. doi:10.1016/j.mpaic.2012.04.010
- Battillo JA, Hendler MA. Effects of patient positioning during anesthesia. *Int Anesthesiol Clin*. 1993;31(1):67-86. doi:10.1097/00004311-199331010-00008
- Akhavan A, Gainsburg DM, Stock JA. Complications associated with patient positioning in urologic surgery. *Urology*. 2010;76(6):1309-1316. doi:10.1016/j.urology.2010.02.060
- Bjoro B, Mykkeltveit I, Rustoen T, Candas Altinbas B, Roise O, Bentsen SB. Intraoperative peripheral nerve injury related to lithotomy positioning with steep Trendelenburg in patients undergoing robotic-assisted laparoscopic surgery - a systematic review. *J Adv Nurs*. 2020;76(2):490-503. doi:10.1111/jan.14271
- Gal J, Hyman J, Gainsburg DM. Positioning for urological procedures. In: Gainsburg D, Bryson E, Frost E, ed. *Anesthesia for Urologic Surgery*. Springer. 2014.
- Katayama S, Mori K, Pradere B, et al. Influence of steep Trendelenburg position on postoperative complications: a systematic review and meta-analysis. *J Robot Surg*. 2022;16(6):1233-1247. doi:10.1007/s11701-021-01361-x
- Tekgöl ZT, Horsanalı BÖ, Horsanalı MO. Anesthesia for urological surgery. *Cur Topics Anesthesiol*. 2017;17:53-97. doi:10.5772/66196
- Ghabra H, Smith SA. Anesthesia for urological procedures. In: Goudra B, ed. *Anesthesiology*. Springer. 2018.
- Yoshida T, Nakamoto T, Kamibayashi T. Ultrasound-guided obturator nerve block: a focused review on anatomy and updated techniques. *Biomed Res Int*. 2017;2017:7023750. doi:10.1155/2017/7023750
- Wu J, Gao Y, Xiong Z, et al. Comparison of different methods of obturator nerve block in transurethral resection of bladder tumors: a systematic review and network meta-analysis. *Cancer Med*. 2023;12(5):5420-5435. doi:10.1002/cam4.5364
- Agin C. Anesthesia for transurethral prostate surgery. *Int Anesthesiol Clin*. 1993;31(1):25-46. doi:10.1097/00004311-199331010-00005
- Rassweiler J, Teber D, Kuntz R, Hofmann R. Complications of transurethral resection of the prostate (TURP)--incidence, management, and prevention. *Eur Urol*. 2006;50(5):969-979. doi:10.1016/j.eururo.2005.12.042
- Jensen V. The TURP syndrome. *Can J Anaesth*. 1991;38(1):90-96. doi:10.1007/BF03009169
- Hawary A, Mukhtar K, Sinclair A, Pearce I. Transurethral resection of the prostate syndrome: almost gone but not forgotten. *J Endourol*. 2009;23(12):2013-2020. doi:10.1089/end.2009.0129
- Schneidewind L, Kranz J, Schlager D, et al. Multicenter study on antibiotic prophylaxis, infectious complications and risk assessment in TUR-P. *Cent European J Urol*. 2017;70(1):112-117. doi:10.5173/ceju.2017.941
- Okmen K, Okmen BM. Ultrasound-guided anterior quadratus lumborum block for postoperative pain after percutaneous nephrolithotomy: a randomized controlled trial. *Korean J Anesthesiol*. 2020;73(1):44-50. doi:10.4097/kja.19175
- Berger JH, Abdou W, Roberts JL, et al. Erector spinae plane blocks for analgesia after percutaneous nephrolithotomy a pathway to reduce opioids. *Can Urol Assoc J*. 2023;17(10):E330-E335. doi:10.5489/auaj.8323
- Knudsen F, Jorgensen S, Bonde J, Andersen JT, Mogensen P. Anesthesia and complications of extracorporeal shock wave lithotripsy of urinary calculi. *J Urol*. 1992;148(3 Pt 2):1030-1033. doi:10.1016/s0022-5347(17)36807-6
- Kofler O, Prueckner S, Weninger E, et al. Anesthesia for open radical retropubic prostatectomy: a comparison between combined spinal epidural anesthesia and combined general epidural anesthesia. *Prostate Cancer*. 2019;2019:4921620. doi:10.1155/2019/4921620
- D'Alonzo RC, Gan TJ, Moul JW, et al. A retrospective comparison of anesthetic management of robot-assisted laparoscopic radical prostatectomy versus radical retropubic prostatectomy. *J Clin Anesth*. 2009;21(5):322-328. doi:10.1016/j.jclinane.2008.09.005
- Whalley DG, Berrigan MJ. Anesthesia for radical prostatectomy, cystectomy, nephrectomy, pheochromocytoma, and laparoscopic procedures. *Anesthesiol Clin North Am*. 2000;18(4):899-917. doi:10.1016/s0889-8537(05)70201-7
- Ozyuvaci E, Altan A, Karadeniz T, Topsakal M, Besik A, Yucel M. General anesthesia versus epidural and general anesthesia in radical cystectomy. *Urol Int*. 2005;74(1):62-67. doi:10.1159/000082712
- Kulkarni JN. Perioperative morbidity of radical cystectomy: a review. *Indian J Urol*. 2011;27(2):226-232. doi:10.4103/0970-1591.82842
- Chen K, Wang J, Dai J, et al. Anesthetic management of radical nephrectomy in patients with renal cell carcinoma involving renal vein or inferior vena cava. *Tumori*. 2019;105(5):411-416. doi:10.1177/0300891619839295
- Cary C, Foster RS, Masterson TA. Complications of retroperitoneal lymph node dissection. *Urol Clin North Am*. 2019;46(3):429-437. doi:10.1016/j.ucl.2019.04.012
- Stephens M, Murphy T, Hendry D. Anaesthesia for retroperitoneal lymph node dissection in the treatment of testicular cancer. *BJA Educ*. 2019;19(9):283-289. doi:10.1016/j.bjae.2019.04.003
- Altas C, Kucukosman G, Yurtlu BS, et al. Anesthesia methods used by anesthetic specialists for circumcision cases. National survey study for Turkey. *Saudi Med J*. 2017;38(1):75-81. doi:10.15537/smj.2017.1.15632
- Adler AC, Bhatia VP, Chandrakantan A, Nathanson BH, Ouellette L, Austin PF. Association of analgesic block with the incidence of complications following hypospadias surgery; a meta-analysis. *Urology*. 2022;166:11-17. doi:10.1016/j.urology.2022.03.002
- Heid F, Jage J. The treatment of pain in urology. *BJU Int*. 2002;90(5):481-488. doi:10.1046/j.1464-410x.2002.02908.x