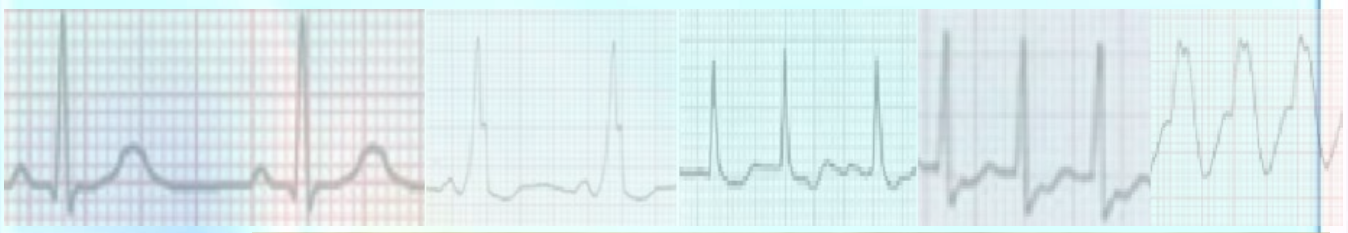
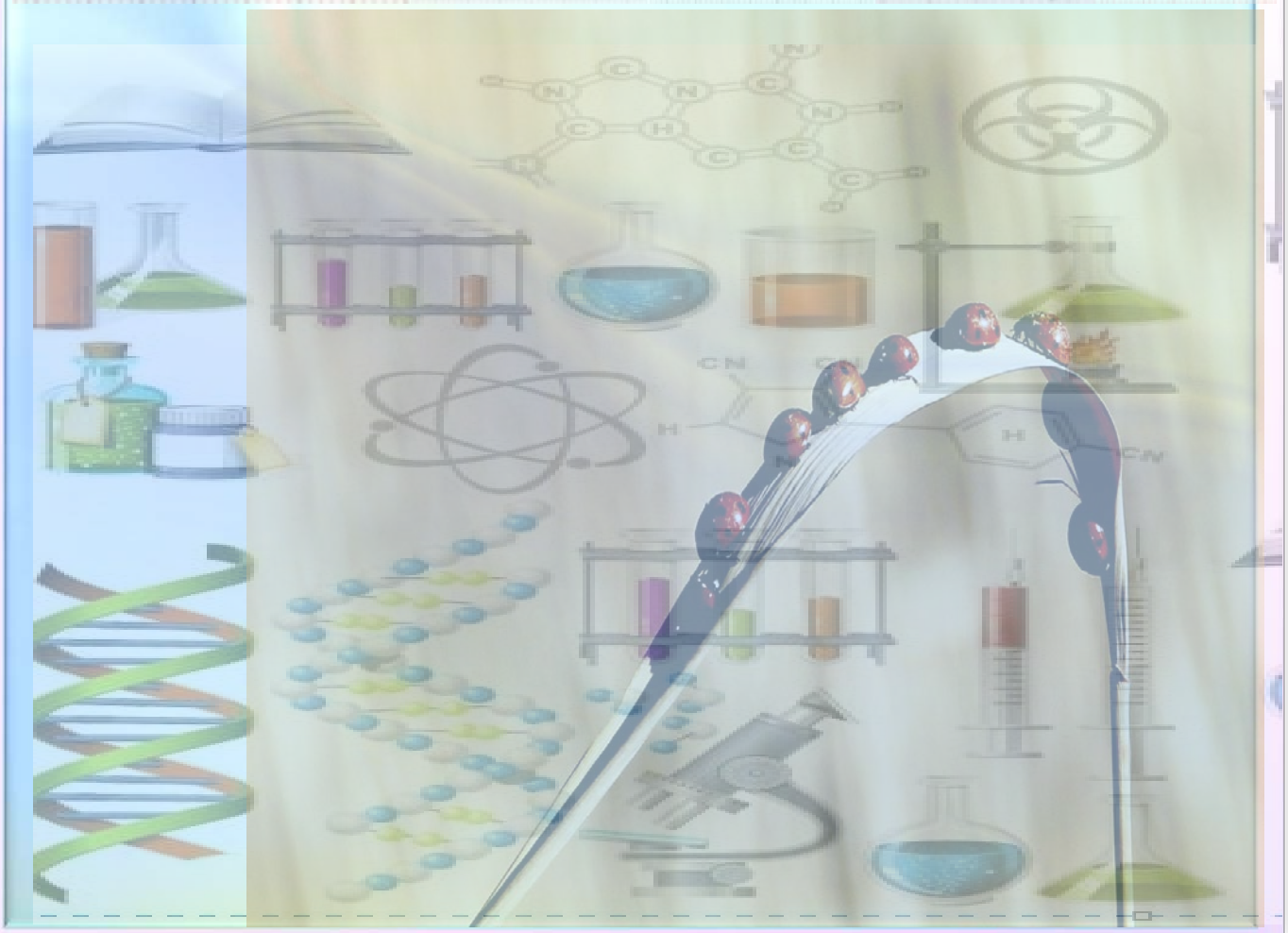
IJCMBS

International Journal of Current Medical and Biological Sciences

Volume 3 Issue 3 December-2023

e-ISSN:2791-8815





Journal Editorial Board

Overview

The International Journal of Current Medical and Biological Sciences is an international, peer-reviewed, open-access electronic and conventional published journal in the English language. The journal accepts clinical and experimental studies, editorial articles, technical and educational reviews, clinical case reports, original images, letters to the editor, and congress abstracts that contribute to general medicine and academic studies.

Information About the Journal

IJCMBS was established in 2021as open access and peer-reviewed journal that accepts articles in English. IJCMBS is published 3 times a year. Articles submitted should not have been previously published or be currently under consideration for publication any place else and should report original unpublished research results. The journal does not expect any fees for publication. All articles are available on the website of the journal with membership.

Journal Management Location and Address

Harran University Faculty of Medicine Osmanbey Campus Haliliye/ SANLIURFA/TURKIYE
Web: https://ijcmbs.com
E-mail: info@ijcmbs.com

Manuscript Preparation Guidelines

Author Guidelines

WRITING RULES

Manuscripts submitted for publication should be written in Microsoft Word. All text, figures and graphics should be sent electronically. Except for the cover page, the name of the institution and the authors should not be mentioned anywhere in the article. The cover page must be loaded separately.

ALL ARTICLES

Title page,
Turkish Abstract,
English Abstract,
Article Section,
Descriptions,
Referances,
Tables,
Figures and Pictures,
It should be arranged as subtitles.

Authors' Open Researcher and Contributor ID **(ORCID ID)** information must be uploaded to the system during article submission.

The article part (except for the abstract, references, table, figure and subtitles) of the research reviews should not exceed **3500 words**, the abstract part should not exceed **250 words,** the references should **not exceed 40**, the number **of tables 5** and the number of **figures 5 should** not exceed. Case reports should consist of Turkish Title, English title, Turkish and English abstract, introduction, presentation of the case(s), discussion and references. Case reports should not exceed **5 pages** in total. Articles on technical and medical developments and image presentations of original topics should not **exceed 3 pages.**

PREPARATION OF ARTICLES

A plain and understandable writing language should be used in the text, scientific writing style should be adopted and unnecessary repetitions should be avoided. Writing; It should be written with 1.5 line spacing, Times New Roman 12 points. Pages should be numbered in the lower right corner. Manuscripts should be uploaded to the system in 2 files.

1 – Title PAGE

The title of the article should not exceed 100 characters (letters) in research articles and 80 characters in case reports. The title should be written in both English and Turkish. The names and surnames of the authors who contributed to the study should be written clearly.
If the study has been presented in any congress before, the congress name, time (day-month-year and congress place) should be specified.
The name, surname, full address, postal code, telephone e-mail address of the author to be contacted should be written at the bottom of the title page. **Reviewer recommendation:** Assists the editor when selecting a referee for a specific study. Include the names and contact details of at least **2 potential reviewer** on the title page.

2- FULL TEXT

The full texts to be reviewed by the referees during the evaluation process should be uploaded to the system as a single file. The full text file should be composed of the following parts and should be arranged in this order.

A) Abstract

Title of the Article; It should be short, easy to understand and describe the content of the article. Turkish (Abstract) and English (Abstract) abstracts should have Turkish and English titles at the beginning. It should not exceed **250** words in research reviews and **150** words in case reports.
Abstracts, Bacground, Materials and Methods, Results, Conclusion, Keywords in Turkish research articles; In English research papers, it should consist of Background, Materials and Methods, Results, Conclusions, Key words sections.
Case reports do not require these sections.
Keywords; At the end of the Turkish Abstract and English Abstract section, under the heading Keywords and Keywords, there should be a maximum of five keywords that capture the main titles of the scientific article and are written in accordance with the Index Medicus Medical Subject Headings (MeSH). Care should be taken to select the keywords from the Science Terms of Turkey (www.bilimterimleri.com).
Abbreviations in the text should be explained in parentheses where they are first used. Abbreviations should not be used in abstracts.

B) Article

It consists of Introduction, Material and method, Results, Discussion and Conclusion sections.
Introduction: Information that will explain the subject and the purpose of the study is given.
Material and method: The place, time, and planning of the study, as well as the elements and methods used, should be reported. Data collection, characteristics of patients and individuals, characteristics of the experimental study, and statistical methods should be explained in detail.
Results: The obtained data should be given together with the statistical results.
Discussion: The results of the study should be evaluated by comparing with the literature data.
All spellings must comply with Turkish spelling rules and must be in accordance with punctuation marks. Abbreviations should be avoided as much as possible. References, figures, tables and pictures should be numbered in the order they appear in the text.
Conclusion: Findings from the study should be reported briefly without adding comments.

C) Referances

References should be written with 1.5 line spacing. Reference numbers should be given in ( ) without a period at the end of the sentence, and the period should be placed later. If more than one reference number is given, “,” should be placed between them, and if more than two consecutive reference numbers are given, “-” should be placed between the numbers [eg. such as (1,2), (1-3)].
If the journal is used as a source: year, volume, issue, start and end pages are given.
If a book is used as a source: only year, start and end pages are given. The surnames and initials of the authors should be written in the references. If the number of authors is **3** or less in the references, all author names are written. If the name of the author is more than **3,** instead of the names of the following authors, "et al." is written in English sources and "et al." in Turkish sources. Journal names should be abbreviated according to Index Medicus. The way of writing the reference should be like the examples below. References should be arranged in the language of the article and as seen in the examples below.
Sources from journals: Tascanov MB, Tanriverdi Z, Gungoren F, et al. Comparisons of microbiota-generated metabolites in patients with young and elderly acute coronary syndrome. Anatol J Cardiol. 2020;24(3):175-82.

Books; 1. Wagner G. S. Marriott's Practical electrocardiography, Tenth ed. Lippincott Williams Publisher, 2000: 124-129

Web article: Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

Website; Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 July 2002]. Available from: www.cancer-pain.org

Thesis; Gezer R: Morphological Characteristics and Individual Differences of Rugae Palatines. Master Thesis, Şanlıurfa: Harran University Institute of Health Sciences, 2016.

D) Explanations

Financial resources, contributing institutions, organizations and individuals, if any, should be specified in this section.

E) Tables

Tables should be written on a separate page with 1.5 line spacing, each table should have a number and an explanatory name. If there are abbreviations in the table, their expansions should be written in alphabetical order under the table. Table numbering (Table 1. , Table 2., ...) should be given consecutive numbers and Roman numerals should not be used. Tables should be uploaded in the article on a separate page.

F) Figures and Pictures

Figures and pictures must be named and numbered. Numbering (Figure 1., Figure 2., …) should be given consecutive numbers and Roman numerals should not be used. Images should be clear and have a minimum resolution of 300 dots per inch (dpi). Images should be uploaded within the article on a separate page. If abbreviations are used under the figure and picture, the explanation of the abbreviations should be stated under the subtitle in alphabetical order. The magnification and technique of microscopic images should be explained. The editorial board can make any changes it deems necessary without changing the essence of the article.

COMPLIANCE WITH PUBLICATION ETHICS

It is a must to prepare the manuscripts in accordance with research and publication ethics. The authors should state that they accept ethical principles in all human clinical research and that they conduct the research in accordance with these principles. Regarding these, in the Materials and Methods section: they obtained approval for each prospective and retrospective study from the ethics committee of the institution where the clinical research was conducted, and they obtained informed consent from the people who participated in the study or their guardians; In experimental studies on animals, they have to state that they protect animal rights and that they have received approval from the relevant experimental animal ethics committee. Regarding the results of experimental studies on humans or experimental animals, it is obligatory to submit an ethics committee approval document during the application to the journal. In the presence of the author(s), commercial link or institution providing financial support for the study; used commercial product, drug, company, etc. should inform the Editor on the presentation page. The absence of such a situation should also be stated on a separate page.

In studies that require ethics committee approval, the Ethics Committee Approval Document should be uploaded to the system during the article submission process, and the information about the permission (board name, date and issue number) should be stated in the material and method section, as well as in the explanations section after the discussion section of the article. Studies that require the approval of the Ethics Committee are as follows.

All kinds of research conducted with qualitative or quantitative approaches that require data collection from the participants by using survey, interview, focus group work, observation, experiment and interview techniques.

Use of humans and animals (including material/data) for experimental or other scientific purposes, Clinical studies on humans, Animal studies,

Retrospective studies in accordance with the law on the protection of personal data, (If requested, the permission document obtained from the institution where the study was carried out should also be uploaded

to the system when the archive is scanned.)
The patient's clear identity should not be shared in the Case Report - Series.

EVALUATION AFTER THE REFEREE'S REPORT

Authors should write the topics that are requested to be corrected in the referee report as an answer in the answer section reserved for them. In addition, they should make the necessary changes in the article and resubmit them online by specifying (painting) them in the article

Contents *Pages*

IJCMBS

THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Letter to The Editor

Can Bacteriophage Therapy Be an Alternative Solution Against Medicinal Leech Associated Infections?

Mustafa Ünal[1*] Muhammed Emin Göktepe[2] Mustafa Yasin Selçuk[1] Onur Öztürk[3]

[1] Ondokuz Mayıs University Faculty of Medicine, Department of Family Medicine, Samsun/TURKİYE

[2] Giresun Education and Research Hospital Department of Family Medicine, Giresun/TURKİYE

[3] Samsun Education and Research Hospital, Department of Family Medicine Samsun/TURKİYE

Abstract

Medicinal leeches are effective in many clinical conditions. But leech associated Aeromonas infections are common and limits the benefits of leech therapy. Bacteriophages are specific bacteria hunting viruses that could be used effectively against target bacteria without side effects. There are 5 bacteriophages defined in the literature against Aeromonas spp. which their clinical use in hiridotherapy associated infections could open a way for a safer and more effective usage of medicinal leeches.

Key Words: Medicinal leeches; hydrotherapy; bacteriophages; Aeromonas infections

Öz

Tıbbi sülükler birçok klinik durumda etkilidir. Ancak sülükle ilişkili Aeromonas enfeksiyonları yaygındır ve sülük tedavisinin faydalarını sınırlar. Bakteriyofajlar, hedef bakterilere karşı yan etkileri olmadan etkili bir şekilde kullanılabilen spesifik bakteri avlayan virüslerdir. Literatürde Aeromonas spp.'ye karşı tanımlanan 5 bakteriyofaj bulunmaktadır. hiridoterapi ile ilişkili enfeksiyonlarda klinik kullanımları, tıbbi sülüklerin daha güvenli ve daha etkili kullanımının yolunu açabilir.

Anahtar Kelimeler: Tıbbi sülükler; hirudoterapi; bakteriyofajlar; Aeromonas enfeksiyonlar

Dear Editor,

Medicinal leeches have been used for various diseases since ancient times (1). They have a numerous valuable protein in their saliva that are beneficial for relieving venous congestion and stimulating wound healing. For these reasons medicinal leeches are being employed for the salvage of flaps and grafts and reimplantation of amputated body parts. It is being reported that they are even useful salvaging the reimplanted body parts where establishing venous anastomosis was not possible (2). Hirudine is the best-known substance in the leech saliva and some hirudine derivatives (lepirudine, bivalirodin and desidurine) are developed for clinical use (3).

Despite the benefits medicinal leech therapy is not risk free and leech associated risks include infections, prolonged bleeding and allergy. Leeches rely on Aeromonas species to digest blood as they provide enzymes for protein breakdown. This commensal relationship makes leeches potential vectors for these microbes and eradication them from the leeches' digestive system is very hard. Overall infection risk for leech therapy is reported as %2-20 and %88 of them are caused by Aeromonas spp. These infections may cause clinical conditions ranging from simple cellulitis to meningitis. They also severely undermine survival of flaps and reimplanted body parts (4).

Effective control of leech ascoitaded infections is very important. First line antibiotics are 3rd. generation cephalosporins, fluoroquinolones and trimethoprim-sulfamethoxazoles. Generally, antibiotics are effective but

***Corresponding author:** *Dr*. Muhammed Emin GÖKTEPE, Ph.D., M.D.

Adress: Giresun Education and Research Hospital Department of Family Medicine, Giresun/TURKİYE

E-mail: drmeg38@gmail.com **Received:** 04.06.2023 **Accepted:** 12.07.2023

Cite as: UNAL.M and at al. Can Bacteriophage Therapy Be an Alternative Solution Against Medicinal Leech Associated Infections?IJCMBS 2023;3(3):138-9 doi.org/ 10.5281/zenodo.8150153

emergence of multi drug resistance strains are reported. Furthermore, antibiotics have some negative effects on microbiome and body flora. Antibiograms from leeches digestive microbes and from the leech tanks are advised (5). But these measures take time, and they may not be very practical. Therefore, treatment of leeches with antibiotics, chlorhexidine and bleach solutions are being proposed. But we may have another potential weapon (bacteriophages) for this problem.

Aeromonas species is well known in marine life as they cause infections in fish and other marine stock that result in economic losses. They also cause infections such as gastroenteritis in humans and leeches introduce Aeromonas directly to blood and other bodily fluids.

Bacteriophages are specific bacteria devouring viruses which were in favor before the discovery of antibiotics. They only target specific bacteria, replicate until target bacteria is annihilated and very rarely cause systemic and local side effects. Small amount could be enough for therapy, and they also don't interfere with the normal flora. With the emergence of antibiotic resistance, phages again started to catch medical communities attention. In literature 5 phages (N21, W3, G65, Y71 and Y81) from Myoviridae ve Podoviridae families are reported against A. hydrophilia (6). Phages can be a viable alternative for the treatment of leech associated infections. If the infections have started in the body, they can provide fast and effective treatment and local introduction of the phages in the affected tissues could be enough as they track down the target bacteria effectively. Alternatively, phages can be introduced into the tank water before leeches applied to the body. Research should be undertaken to determine the best way of using these bacteria hunters that would make leech therapy safer.

Acknowledgements*: none*

Author Contributions: *Concept: MEG, Literature Review: MÜ, Design: OÖ,MEG, Data acquisition: MÜ, Analysis and interpretation:MYS, Writing manuscript: OÖ,MÜ Critical revision of manuscript: MEG,MSY.*

Conflict of Interest: *The author has no conflicts of interest to declare.*

Financial Disclosure: *Author declared no financial support.*

References

1. Giacometti L. Leeching in the twentieth century. Am J Cardiol. 1987;60(13):1128-31.
2. Hackenberger PN, Janis JE. A Comprehensive Review of Medicinal Leeches in Plastic and Reconstructive Surgery. Plast Reconstr Surg Glob Open. 2019;7(12):e2555.
3. Corral-Rodríguez MA, Macedo-Ribeiro S, Pereira PJ, et al. Leech-derived thrombin inhibitors: from structures to mechanisms to clinical applications. J Med Chem. 2010;53(10):3847-61.
4. Sig AK, Guney M, Uskudar Guclu A, et al. Medicinal leech therapy-an overall perspective. Integr Med Res. 2017İ(4):337-43.
5. Verriere B, Sabatier B, Carbonnelle E, et al. Medicinal leech therapy and Aeromonas spp. infection. Eur J Clin Microbiol Infect Dis. 2016;35(6):1001-6.
6. Liu, J, Gao, S, Dong, Y. et al. Isolation and characterization of bacteriophages against virulent Aeromonas hydrophila. BMC Microbiol 2020;(20), 141.

IJCMBS

THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Letter to The Editor

The Usability of IVC Diameter, IVC Collapsibility Index and Snuffbox Resistive Index in the Management of Sepsis and Septic Shock Patients in the Emergency Department

Acil Serviste Sepsis ve Septik Şok Hastalarının Yönetiminde IVC Çapı, IVC Kollapsibilite Indeksi ve Enfiye Çukuru Rezistif Indeksinin Kullanılabilirliği

Serdar Özdemir[1*]

[1] Department of Emergency Medicine, University of Health Sciences Ümraniye Training and Research Hospital, Istanbul /TURKİYE

Dear Editor,

Hemodynamics is a science that studies the properties and rules of movement of blood and its components in the body. Oxygen delivery to tissues is an important component of peripheral and systemic circulatory hemodynamics. Peripheral and systemic circulation is the key point to achieve hemodynamic stability. Hemodynamic evaluation guides the admission of patients to the intensive care unit during the diagnosis and treatment process (1).

Early recognition of sepsis, which has high mortality and morbidity rates, and initiation of early treatment are vital. Adequate fluid resuscitation is essential in the treatment of sepsis. Most patients may require large amounts of fluid support depending on the hemodynamic response. Normalization of lactate levels can be used as a guide for adequate fluid resuscitation (2). Bedside cardiac ultrasonography and other techniques can be used to assess fluid response. According to recent studies on the physiopathology of sepsis, macro and microcirculation issues have gained great importance. With the development of ultrasound technology, the study of peripheral blood flow and the treatment and patient management of entities such as sepsis have focused on these areas (3). In the sepsis guideline, an important part of the treatment is to give the patient early intensive fluid therapy. Early intervention rather than interventions in treatment provides a reduction in mortality. Therefore, early aggressive fluid therapy has an important place in the follow-up of sepsis (2).

IVC is a vessel with high compliance. Intrapleural pressure changes within the respiratory cycle and measurements of IVC diameter have been tried to be correlated with volume in many studies. Ultrasound evaluation of the inferior vena cava has been used for many years. The inferior vena cava collapsibility index is calculated by recording the diameters in the inspiration and expiration of the measurements. This measurement method has been found to be successful and effective in fluid resuscitation. The width and collapsibility of IVC diameter vary with total body fluid and respiratory pattern. Studies have shown that IVC diameter is related to intravascular volume rather than systolic blood pressure, and this has been used to determine fluid requirement and after shock (4,5). Nette et al. showed that systolic pressure increased but there was no significant change in IVC diameter in their study in patients receiving hemodialysis with low blood volume infused with norepinephrine. This suggested that IVC diameter measurements may be closely related to intravascular volume (6). Trivedi et al. reported that for the assessment of fluid status and fluid responsiveness in end-stage renal disease patients with maintenance hemodialysis, ultrasound assessment of IVC diameter and IVC collapsibility index are not routinely helpful in a review of 60 patients (7). A meta-analysis by İsmail et al. revealed that the IVC collapsibility index has a moderate level of evidence in the recognition of euvolemic and hypovolemic states (8).

The Resistive Index (RI) is a flow parameter calculated on USG, based on the minimum and maximum. Doppler measurement of a vessel within the heartbeat cycle. It can show collapsibility as well as resistance within the vessel. Formula of RI is (Peak Systolic Velocity- Peak End Diastolic Velocity) /Peak Systolic Velocity. As the vessel contracts, the resistance to the flow increases and RI increases. Since it is a multifactorial value, it can have different normal values in each organ and in each vein. In the

***Corresponding author:** *Dr. Serdar Özdemir*, M.D.

Adress: Department of Emergency Medicine,University of Health Sciences Ümraniye Training and Research Hospital, Istanbul /TURKİYE

E-mail: dr.serdar55@hotmail.com **Received:** 12.06.2023 **Accepted:** 15.07.2023

Cite as: OZDEMİR.S The Usability of IVC Diameter, IVC Collapsibility Index and Snuffbox Resistive Index in the Management of Sepsis and Septic Shock Patients in the Emergency Department. IJCMBS 2023;3(3):140-1 doi.org/10.5281/zenodo.8150571

study of Ban et al. in 2005 published in circulation journal, correlation in the resistance of the peripheral circulation was investigated by using the resistive index of the upper extremity arteries in intensive care patients whose systemic vascular resistance was measured invasively. They reported a significant correlation in RI's showing this resistance (9). In the same study, measurements were made from the brachial, radial artery, and the radial artery passing through the snuffbox. Due to the narrow angle of ultrasound, it provides, the measurements in the snuff pit gave the best correlation. In another study conducted with the snuffbox resistive index (SBRI), it was shown that it is parallel to the change in lactate clearance and can be used in tissue perfusion and treatment, diagnosis, and follow-up in septic shock (10). In the light of current literature, SBRI could be another ultrasonographic useful parameter in diagnosis of sepsis and septic shock.

In conclusion, more blinded studies are needed to safely recommend SBRI, IVC diameter and IVC collapsibility index in the management of sepsis and septic shock patients in the emergency department. Researchers should be encouraged to study the usability of SBRI, IVC diameter and IVC collapsibility index in the management of sepsis and septic shock patients in the emergency department.

Acknowledgements*: none*

Author Contributions: *Concept:SÖ, Literature Review: SÖ, Design: SÖ, Data acquisition: SÖ, Analysis and interpretation: SÖ, Writing manuscript: SÖ, Critical revision of manuscript: SÖ.*

Conflict of Interest: *The author has no conflicts of interest to declare.*

Financial Disclosure: *Author declared no financial support.*

References

1. Özkan A. Comparison of the c-reactive protein-mean arterial pressure ratio with critical care prognostic scoring systems. Ann Clin Anal Med 2022;13(11):1257-61.
2. Taşlıdere B, Sönmez E, Coşkun A. Can Sepsis-Induced Coagulopathy Scores and Routine Blood Tests Indicate Prognosis in Patients with COVID-19? Bezmialem Science 2023;11(2):189-94.
3. Singer M, Deutschman CS, Seymour C, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315(8):801–10.
4. İnce M, Ocak M. The Most Useful Method to Evaluate the Volume Status Of Critical Patients In The Emergency And Intensive Care Units: Point Of Care Ultrasound. J Contemp Med. 2020; 10(4): 474-80.
5. Özbek AE, Karakayalı O. Comparison of Inferior Vena Cava Collapsibility and Clinical Scales for the Assessment of Dehydration in Children with Diarrhea. Anatolian J Emerg Med. 2022; 5(3): 133-138.
6. Nette RW, Ie EHY, Vletter WB, et al. Norepinephrine-induced vasoconstriction results in decreased blood volume in dialysis patients. Nephrol Dial Transplant. 2006;21(5):1305–11.
7. Trivedi V, Prajapati M, Prajapati DJ, et al. Is Inferior vena cava diameter, a reliable indicator for fluid status in end-stage renal disease patients? - A prospective observational study. Indian J Transplant 2022; 16:200-4.
8. Ismail MT, El-Iraky AA, Ibrahim EEA, et al. Comparison of inferior vena cava collapsibility and central venous pressure in assessing volume status in shocked patients. Afr J Emerg Med. 2022;12(3):165-71.
9. Ban K, Kochi K, Imai K, et al. Novel Doppler technique to assess systemic vascular resistance: the snuffbox technique. Circ J. 2005 Jun;69(6):688-94.
10. Wang C, Wang X, Zhang H, Su L, et al. Association Between Doppler Snuffbox Resistive Index and Tissue Perfusion in Septic Patients. Shock. 2020;54(6):723-30

IJCMBS

THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Case Report

Bilateral Ureteral Involvement in Endometriosis - Case Report

Bilateral Üreter Tutulumu Olan Endometriozis: Olgu Sunumu

Musab Köse*[1], Arda Tongal[1], Ali Nihat Gökcan[1], Mehmet Gündoğan[2], Erkan Arslan[1], Hakan Türk[1]

[1]Department of Urology, Uşak University, Training and Research Hospital, Usak, Türkiye

[2]Department of Pathology, Uşak University, Training and Research Hospital, Usak,Türkiye

*Corresponding author:

Dr. Musab Köse M.D

Address:

Department of Urology, Usak University, Training and Research Hospital, 64300, Usak, Türkiye

E-mail: musabks@gmail.com

Received:04/06/2023

Accepted: 28/08/2023

Cite as: KOSE. M and et al. Bilateral Ureteral Involvement in Endometriosis - Case Report. IJCMBS 2023;3(3):142-6 doi.org/ 10.5281/zenodo.10020757

Highlights

- Ureteral endometriosis is a rare pathology that, if left untreated, can lead to renal damage.
- It should be considered in the differential diagnosis of resistant ureteral obstructions.
- Surgical intervention is the primary treatment for cases where obstruction develops due to ureteral endometriosis.

Abstract

Ureteral endometriosis is a rare pathology that, if left untreated, can lead to renal damage. In this case, we present a 48-year-old female patient with a rare persistent bilateral ureteral obstruction and hydroureteronephrosis.

Imaging revealed the obstruction but was not helpful in illuminating the etiology. In the patient who underwent exploratory laparotomy, the affected ureter and surrounding fibrotic foci were resected, and ureteroneocystostomy was performed. During follow-up, the patient's clinical condition improved, and no recurrence was observed.

Consequently, ureteral endometriosis is a rare pathology, and imaging may not be helpful in determining the etiology. It should be considered in the differential diagnosis of resistant obstructions.

Keywords: Ureteral endometriosis, upper urinary tract obstruction, obstructive uropathy

ÖZ

Üreteral endometriozis, tedavi edilmediği takdirde böbrek hasarına yol açabilen nadir bir patolojidir. Bu vakada, nadir görülen bilateral üreter obstrüksiyonu ve hidroüreteronefrozu olan 48 yaşında bir kadın hastayı sunuyoruz.

Görüntüleme yöntemleri obstrüksiyonu ortaya çıkardı ancak etiyolojiyi aydınlatmada yardımcı olmadı. Eksploratuvar laparotomi yapılan hastada etkilenen üreter ve çevresindeki fibrotik odaklar rezeke edilerek üreteroneosistostomi uygulandı. Takiplerinde hastanın klinik durumu düzeldi ve nüks gözlenmedi.

Sonuç olarak üreteral endometriozis nadir görülen bir patolojidir ve görüntüleme etiyolojiyi belirlemede yardımcı olmayabilir. Dirençli obstrüksiyonların ayırıcı tanısında düşünülmelidir.

Anahtar Kelimeler: Üreteral endometriozis, üst üriner sistem obstrüksiyonu, obstrüktif üropati

Introduction

Endometriosis is a chronic inflammatory pathology that is seen in approximately 10% of women in the reproductive period and it is characterized by pain and adhesion of the endometrial layer outside the uterus (1). Ureteral involvement of endometriosis, which also has atypical involvements such as gastrointestinal tract, lung, liver, pericard and brain is a rare but serious clinical form. According to research conducted in Europe, the prevalence of urinary tract endometriosis (UTE) varies between 0.3% and 12% among people affected by endometriosis, and between 20% and 52.6% among women with deep endometriosis (2, 3). Extrapelvic endometriosis most commonly affects the urinary system after the gastrointestinal tract, with the bladder being the most affected site in 85% of women with UTE, followed by the ureter at 10%, kidney at 4%, and urethra at 2% (4, 5). When it is located around the ureter, it may cause ureteral obstruction and secondary renal failure.

In this case, we present a 48-year-old female patient with a rare persistent bilateral ureteral obstruction and hydroureteronephrosis.

Case Presentation

The patient presented with pain in bilateral flank, abdominal and groin areas, weakness, fatigue, and pollakiuria. Ultrasound (USG) revealed bilateral grade 3 hydroureteronephrosis. Creatinine was 1.15.

In the non-contrast abdominal computed tomography (CT) of the patient, bilateral hydronephrosis was seen, with prominent dilation of approximately 2/3 of both proximal ureters. The distal part was normal on both sides. Subsequently, CT urography was performed with the aim of excluding potential malignancies. The CT urography results demonstrated bilateral ureteral dilation up to the level of the iliac crosses, with normal distal portions. As a result, a diagnostic ureterorenoscopy (URS) was scheduled.

In URS, a circular stenosis was seen in the middle parts of both ureters, and both proximal ureters were dilated. No additional pathology was seen. Double J Stents (DJS) were placed on both sides.

DJS were removed after 75 days. One month later, the patient was admitted to our clinic again with nausea. In the pelvic doppler USG of the patient who had a history of endometriosis; the right ovary size was increased and measured as 55x40 mm. In the right ovary, two cysts were observed measuring 35x25 mm and 20 mm with no vascularization, which may be compatible with the follicle.

The magnetic resonance (MR) urography **(Figure 1)** did not reveal any additional pathological findings or malignancy-related involvement distal to the dilated portion of the ureter.

Figure 1.T2 MRI UROGRAPHY sequence image showing bilateral hydro-uretero-nephrosis secondary to ureteral stenosis. ***(The stenotic segments have been marked)***

On MR urography, a cystic lesion was observed in the right adnexal region extending to the level of the cul-de-sac, measuring 47x27 mm at its widest point with T1A hypointense and T2A hyperintense features. The lesion contained septations but did not show any post-contrast pathological enhancement. Additionally, a T1A hyperintense and T2A hypointense lesion, measuring approximately 2 cm, was observed superior to the aforementioned lesion, which was consistent with a hemorrhagic cyst - endometrioma and did not show contrast enhancement in the post-contrast series.

Exploration was planned on the patient according to the data in the hand.

The patient was positioned in the supine position under general anesthesia. The abdomen was reached with a midline incision under the umbilicus. Two fixed fibrotic lymph nodes with a retracting appearance surrounding both ureters in a circular form were removed. The fibrotic parts of both ureters were removed and ureteroneocystostomy was performed using the Boari-flap and psoas-hitch method. DJS were placed in both ureters.

Pathology Result: Diffuse endometriosis and fibrosis were observed in the surrounding tissues of both ureteral segments that were removed**. (Figure 2)**

Follow-up: After 75 days, both DJS were removed. The patient did not have any symptoms or complaints during the 2-month follow-up. Our patient has been followed for 8 months without any problem.

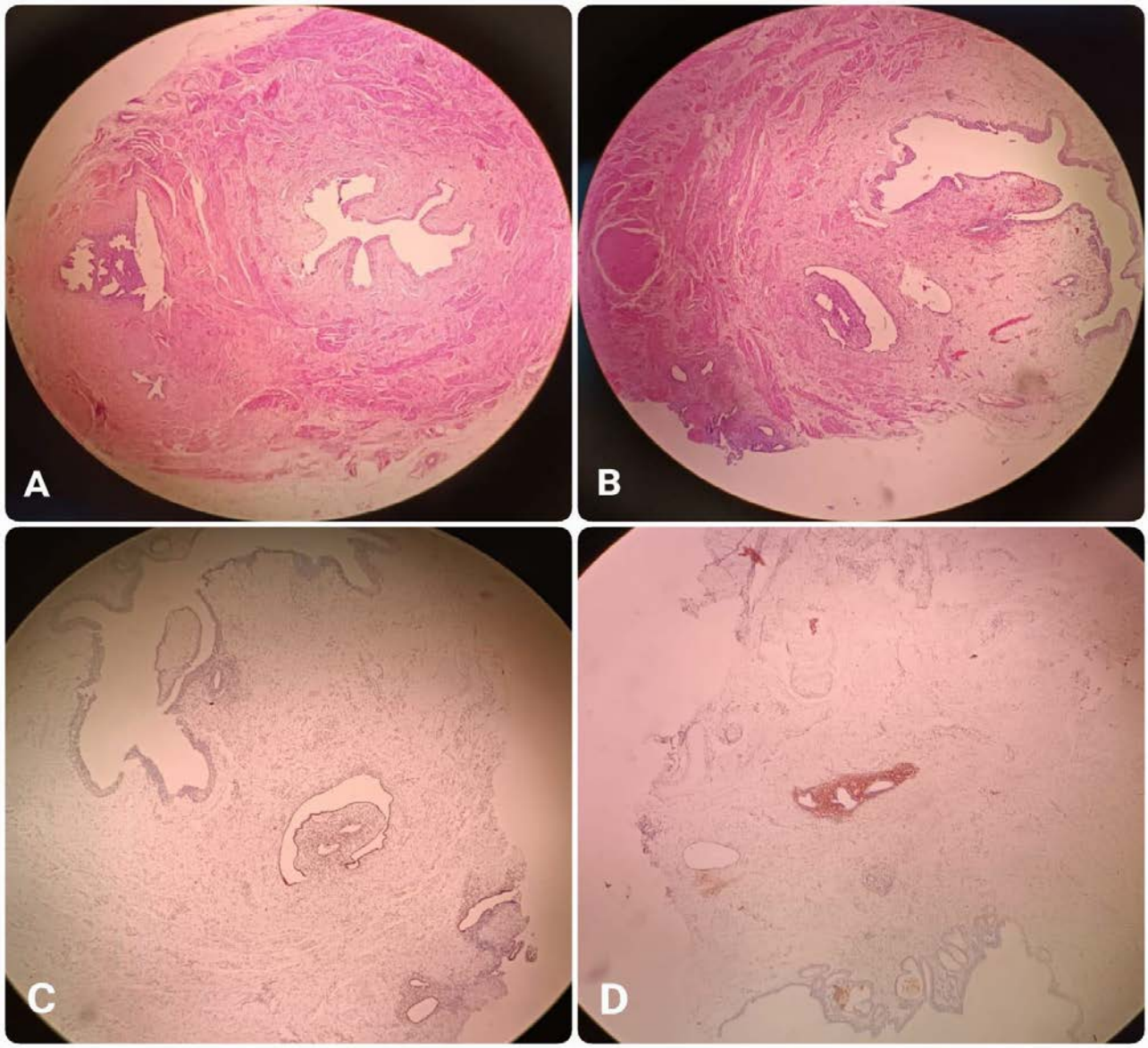


Figure2. Endometriosis foci in surrounding tissue adjacent to the ureteral segments. ***A-B: An endometriosis focus located on the left and ureteral tissue on the right side. (H&E; x 40).C: Endometrial epithelium staining positive with anti-estrogen antibody(x40).D: Endometrial stroma staining positive with anti-CD10 antibody (x40)***

Discussion

The incidence of genitourinary system involvement in endometriosis is 1-2% (6). The most commonly involved organ in the urinary system is the bladder while ureter, kidneys and urethra may also be involved (7).
Ureteral involvement can be histologically classified into two groups based on the type of involvement, namely extrinsic and intrinsic involvement (7). Extrinsic involvement refers to the presence of endometriosis in the periurethral tissue, while intrinsic involvement refers to the occurrence of endometriosis in the muscularis propria, lamina propria, and ureter lumen.
Early identification and treatment of this rare entity is crucial, given the potential risk of clinical progression to renal failure resulting from delayed diagnosis and treatment due to nonspecific symptoms and partial obstruction. Clinicians' awareness of the diagnosis and treatment of ureteral involvement can reduce associated morbidities. In the present case, the diagnosis was made after 9 months from the onset of symptoms.
Regarding the clinical manifestation of endometriosis, the symptoms are dependent on the location and extent of the endometrial tissue, and primarily comprise chronic pelvic pain, dysmenorrhea, deep dyspareunia, cyclical bowel complaints, fatigue, and infertility. In a relevant study, urinary symptoms were reported in only 15.9% of the patients. In our case, the patient's symptoms at admission were characterized by bilateral flank pain radiating to the abdomen and groin, as well as pollakiuria.
Imaging has an important place in the diagnosis of the disease. USG and IV urography are cheap and safe methods, they may be preferred in the first place. CT and MR urography are important because they are guiding for surgery and evaluating other possible diagnoses. In particular, magnetic resonance imaging (MRI) can detect even small endometrial foci (8). But in our case, it could not help the diagnosis. However, if clinical suspicion persists, endometriosis should still be considered.
Imaging plays a crucial role in the diagnosis of endometriosis. The initial assessment is performed USG and intravenous urography due to their cost effectivity and safety. However, CT and MR urography hold significance in guiding surgical intervention and evaluating other potential diagnoses. Of these, MRI is particularly useful at detecting smaller endometrial lesions. Nevertheless, in our case, it was not effective in aiding the diagnosis. Endometriosis should still be considered as a possible diagnosis in case of ongoing clinical suspicion.
Silloe et al. used the degree of contact between the ureter and endometriosis lesions in a study investigating the efficacy of MRI in distinguishing whether ureteral involvement is intrinsic or extrinsic, and they evaluated other MRI findings such as periureteral fat signal changes, the presence of parametrial nodules, and external ureteral compression of the lesion in contact with the ureter (9). In the same study, they compared MRI and surgery to distinguish between intrinsic and extrinsic involvement and concluded that MRI was more sensitive (91%-82%) but less specific (59-67%). In our case, MRI did not assist in diagnosis.
Treatment of ureteral endometriosis is primarily consists of resolvement of obstruction, prevention of renal injury and preservation of function.
One of the treatment alternatives for endometriosis is medical therapy which includes progestogens and GNRH agonists. On the other hand, this therapy which is indicated for early stage disease has an incomplete response and high recurrence rates after the discontinuation of therapy (10). Medical treatment should never delay surgical treatment in a condition such as hydronephrosis which may cause kidney injury (11). We planned surgical treatment on our case as soon as possible due to the bilateral hydroureteronephrosis and high creatinine levels.
In the surgical approach, which is a more permanent and definitive solution in the treatment of obstruction, the options are ureterolysis, ureteroureteral anastomosis and ureteroneocystostomy. The decision of which method will be used is determined according to the patient. Ureterolysis is indicated as the first choice in mild extrinsic cases. However, in case of intrinsic involvement uretero-ureteral anastomosis can be considered in limited involvement with the possibility of preserving the ureter (7). But high recurrence rates have been reported in this technique (12). The other option, ureteroneocystostomy, is particularly indicated in cases where the ureterovesical junction is involved and the uninvolved part of the distal end of the ureter is 1 cm or less (13). In our case, we removed the tissue surrounding the ureter in a circular manner and the fibrotic ureter at the lower end of both ureters. Then we performed ureteroneocystostomy.

Conclusion

As a result, ureteral endometriosis is a rare disease that is difficult to diagnose because of its non-specific symptoms. Suspecting the disease in the presence of associated symptoms is important in diagnosis. MRI is the gold standard for diagnosis and surgery is the most effective treatment option. Increasing awareness of this disease which can lead to kidney loss if its diagnosis is missed has a key role in achieving better results.

Acknowledgements: *none*

Ethical Approval: *none*
Author Contributions: *Concept: HT Literature Review: EA, AT Design: MK Data acquisition: ANG Analysis and interpretation: MG Writing manuscript: MK Critical revision of manuscript: HT*
Conflict of Interest: *The author(s) do not have any potential conflict of interest regarding the research, authorship and/or publication of this article.*
Financial Disclosure: *This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.*

References

1. Greene R, Stratton P, Cleary SD, et al. Diagnostic experience among 4,334 women reporting surgically diagnosed endometriosis. Fertil Steril. 2009;91(1):32-9.
2. Knabben L, Imboden S, Fellmann B, et al. Urinary tract endometriosis in patients with deep infiltrating endometriosis: prevalence, symptoms, management, and proposal for a new clinical classification. Fertil Steril. 2015;103(1):147-52.
3. Gabriel B, Nassif J, Trompoukis P, et al. Prevalence and management of urinary tract endometriosis: a clinical case series. Urology. 2011;78(6):1269-74.
4. Maccagnano C, Pellucchi F, Rocchini L, et al. Ureteral endometriosis: proposal for a diagnostic and therapeutic algorithm with a review of the literature. Urol Int. 2013;91(1):1-9.
5. Berlanda N, Vercellini P, Carmignani L, et al. Ureteral and vesical endometriosis. Two different clinical entities sharing the same pathogenesis. Obstet Gynecol Surv. 2009;64(12):830-42.
6. Comiter CV. Endometriosis of the urinary tract. Urol Clin North Am. 2002;29(3):625-35.
7. Bahall V, Hosein Y, Konduru S, et al. Isolated Intrinsic Ureteral Endometriosis: A Rare Presentation of Ureteral Obstruction. Cureus. 2021; 20;13(10):e18919.
8. Cimsit C, Yoldemir T, Guclu M, et al. Susceptibilityweighted magnetic resonance imaging for the evaluation of deep infiltrating endometriosis: preliminary results. Acta Radiol. 2015. pii: 0284185115602147.
9. Sillou S, Poirée S, Millischer AE, et al. Urinary endometriosis: MR imaging appearance with surgical and histological correlations. Diagn Interv Imaging 2015; 96:373-81.
10. Palla VV, Karaolanis G, Katafigiotis I, et al. Ureteral endometriosis: A systematic literature review. Indian J Urol. 2017;33(4):276-282.
11. Barra F, Scala C, Biscaldi E, et al. Ureteral endometriosis: a systematic review of epidemiology, pathogenesis, diagnosis, treatment, risk of malignant transformation and fertility. Hum Reprod Update. 2018 Nov 1;24(6):710-730..
12. Antonelli A. Urinary tract endometriosis. Urologia. 2012;79(3):167-70.
13. Gehr TW, Sica DA. Case report and review of the literature: ureteral endometriosis. Am J Med Sci. 1987;294(5):346-52.

IJCMBS

THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Orgınal Article

Artificial Intelligence Evaluation of the Utility of HALP Score and Hematological Indicators in Estimating No-Reflow After Primary Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction

ST Segment Yükselmeli Miyokard İnfarktüsü Olan Hastalarda Primer Perkütan Koroner Müdahale Sonrası Yeniden Akım Olmamasını Tahmin Etmede HALP Skoru ve Hematolojik Göstergelerin Faydasının Yapay Zeka ile Değerlendirilmesi

Rustem Yilmaz[1]

[1]Department of Cardiology, Faculty of Medicine, Samsun University, Samsun, Turkiye

*Corresponding author:
Dr. Rustem Yilmaz, MD.

Adress: Samsun University Faculty of Medicine, Samsun Training and Research Hospital, Department of Cardiology, Samsun, Turkiye

E-mail:
drrustemyilmaz@hotmail.com.

Received:11/10/2023
Accepted: 28/10/2023

Cite as: Yılmaz.R. Artificial Intelligence Evaluation of the Utility of HALP Score and Hematological Indicators in Estimating No-Reflow After Primary Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction. IJCMBS 2023;3(3):147-55 doi.org/ 10.5281/zenodo.10020501

Highlights

- In recent studies, artificial intelligence applications are increasingly used in cardiology clinical research.
- Hematological parameters are effective in estimating no-reflow in patients with ST-segment elevation myocardial infarction.

Abstract

Background: Acute Myocardial Infarction (AMI) is a leading cause of mortality globally, with ST-segment Elevation Myocardial Infarction (STEMI) being a specific type. The study aims to fill the gap in literature regarding the predictive utility of hematological parameters and the HALP score in the context of the "no-reflow" phenomenon in STEMI patients. To evaluate the predictive efficacy of hematological parameters and the HALP score in identifying the "no-reflow" phenomenon in STEMI patients undergoing Primary Percutaneous Coronary Intervention (PPCI) using Explainable AI (XAI) methodologies. **Material and Methods:** A retrospective observational design was used, involving 232 STEMI patients who underwent PPCI between January 2020 and September 2023. The cohort was subsequently dichotomized into two subsets based on the presence or absence of the no-reflow phenomenon. Data were collected on demographic variables, MI locations, and hematological parameters. The HALP score was calculated, and XGBoost machine learning models were developed and evaluated. **Results:** Statistically significant differences were observed in white blood cell count (WBC), monocyte (MO), neutrophil (NEU), platelet (PLT), albumin (ALB), and the MPV/LY ratio (MPVLR) between the 'NORMAL-REFLOW' and 'NO-REFLOW' categories. The XGBoost model showed good performance in the training set but had limitations in sensitivity in the test set. **Conclusion:** In this study, according to artificial intelligence analysis, the most important hematological parameter in predicting no-relow was MPVLR. However, in this study, HALP score was not found to be effective in predicting no-reflow. The study provides valuable insights into the predictive factors for reflow outcomes in STEMI patients.

Keywords: Acute Myocardial Infarction, ST-segment Elevation Myocardial Infarction, No-reflow Phenomenon, Hematological Indices, Explainable Artificial Intelligence.

ÖZ

Amaç: Akut Miyokard İnfarktüsü (AMI), dünya genelinde önde gelen ölüm nedenidir ve ST-segment elevasyonlu Miyokard İnfarktüsü (STEMI), akut myokard infartüsünün alt tipidir. Bu çalışma, STEMI hastalarında "yeniden akış olmaması" fenomeni bağlamında hematolojik parametrelerin ve HALP skorunun öngörücü faydasına ilişkin literatürdeki boşluğu doldurmayı amaçlamaktadır. Açıklanabilir Yapay Zeka (XAI) metodolojileri kullanılarak Primer Perkütan Koroner Müdahale (PPCI) uygulanan STEMI hastalarında "yeniden akış olmaması" fenomeninin öngörülmesinde hematolojik parametrelerin ve HALP skorunun öngörücü etkinliğini değerlendirmektir.

Gereç ve Yöntem: Ocak 2020 ile Eylül 2023 arasında PPCI uygulanan 232 STEMI hastasını içeren retrospektif bir gözlem tasarımı kullanıldı. Daha sonra kohort, yeniden akış olmaması fenomeninin varlığına veya yokluğuna dayalı olarak iki alt gruba ayrıldı. Demografik değişkenler, MI lokasyonları ve hematolojik parametrelere ilişkin veriler toplandı. HALP puanı hesaplandı ve XGBoost makine öğrenimi modelleri geliştirilip değerlendirildi. **Bulgular:** 'NORMAL YENİDEN AKIŞ' ve 'YENİDEN AKIŞ OLMAMASI' kategorileri arasında beyaz kan hücresi sayısı (WBC), monosit (MO), nötrofil (NEU), trombosit (PLT), albümin (ALB) ve MPV/LY oranında (MPVLR) istatistiksel olarak anlamlı farklılıklar gözlendi.. XGBoost modeli, eğitim setinde iyi bir performans gösterdi ancak test setinde hassasiyet konusunda sınırlamalar vardı. **Sonuçlar:** Bu çalışmada, yapay zeka analizlerine göre, yeniden akış olmamasını öngörmede en önemli hematolojik parametre MPVLR idi. Ancak bu çalışmada HALP skorunun yeniden akış olmamasını öngörmede etkili olmadığı görüldü. Çalışma, STEMI hastalarında yeniden akış sonuçlarının öngörücü faktörleri hakkında değerli bilgiler sağlıyor.

Anahtar Kelimeler: Akut Miyokard İnfarktüsü, ST-segment elevasyonlu Miyokard İnfarktüsü, Yeniden Akım Olmaması Olayı, Hematolojik İndeksler, Açıklanabilir Yapay Zeka.

Introduction

Acute Myocardial Infarction (AMI) remains a critical public health issue, serving as a leading cause of mortality worldwide. With an annual incidence exceeding three million cases, AMI presents a substantial burden on healthcare systems globally (1-3). The condition is primarily classified into two distinct categories: ST-segment Elevation Myocardial Infarction (STEMI) and Non-ST-segment Elevation Myocardial Infarction (NSTEMI). These classifications are based on the specific ischemic conditions they induce, which arise from either partial or complete cessation of coronary blood flow, culminating in irreversible myocardial damage (4). The clinical consequences of AMI are diverse and severe, ranging from systolic and diastolic cardiac dysfunction to the onset of life-threatening arrhythmias. Additionally, AMI can precipitate severe mechanical complications, such as left ventricular free wall rupture and heart valve dysfunction. The importance of timely coronary reperfusion has been empirically substantiated, showing significant reductions in these complications, particularly within the critical window of the first six hours post-onset (4).

In the specialized field of coronary angiography, the "no-reflow" phenomenon is characterized by a marked reduction in antegrade flow in the coronary artery. This is quantified by a Thrombolysis in Myocardial Infarction (TIMI) flow grade of ≤ 2 and occurs in the absence of any mechanical obstruction following recanalization (5-7). This phenomenon has been empirically linked to both short-term and long-term morbidity and mortality in patients diagnosed with STEMI who are undergoing Primary Percutaneous Coronary Intervention (PPCI).

The three main mechanisms that cause no-reflow are ischemic injury, reperfusion injury and distal embolization (8). First, ischemia causes degeneration of endothelial and myocardial cells. Endothelial cells show folds towards the lumen, bubbles form within the lumen, and the cells show swelling (9). This swelling causes obstruction in the microvascular structure. Necrosis in endothelial cells creates clefts between cells. Erythrocytes leaking from these slits put pressure on the vessels from the outside (10). Ischemia increases the expression of adhesion molecules on the endothelial surface, but decreases nitric oxide synthesis, impairing endothelium-dependent vasodilation. As a result, a thrombus-prone environment and vasospasm occur. The oxygen brought by blood returning to the environment through mechanical or pharmacological reperfusion is repeatedly reduced in the ischemic environment, causing the formation of free oxygen radicals (11). In addition, with the opening of the obstruction, abundant neutrophils cause an inflammatory environment and platelets cause a thrombotic environment. Neutrophils accelerate the production of free oxygen radicals. With the increase in adhesion molecules, neutrophils are taken into the endothelial lumen and reach the intercellular region and cardiac smooth muscle cells (12). Together with the erythrocytes leaking here, they cause interstitial bleeding and vascular compression. In addition, platelets and neutrophils, which come into the environment in large quantities, form microplugs in the capillary circulation. Fragments broken off from the thrombus formed in the lumen cause emboli in the distal vessels and capillaries (13). As a result, reflow cannot be achieved even though there is no mechanical obstruction.

Recent advancements in medical research have shed light on the prognostic utility of specific hematological indices, such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume-to-Lymphocyte Ratio (MPVLR), in predicting adverse outcomes in STEMI patients (14-18). Concurrently, the Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score has emerged as a robust indicator of various clinical outcomes across a spectrum of diseases, including but not limited to, oncological conditions and cardiovascular diseases (19-22).

Despite these advancements, a significant gap exists in the current literature regarding the combined predictive utility of these hematological parameters and the HALP score in the context of no-reflow in STEMI patients. Moreover, no study to date has employed interpretable Artificial Intelligence (AI) methodologies to address this research question.

Machine learning (ML) is a branch of artificial intelligence (AI) that uses data-driven learning to create predictions about new data when exposed to new data. AI/ML approaches are one of the technologies that have seen widespread usage in illness detection and clinical decision support systems in recent years, and they have a wide range of applications. ML, which has a wide range of applications in health, is the foundation of applications in the determination of genetic illnesses, early detection of malignant diseases, and pattern recognition in medical imaging (23,24). ML methods, which are highly preferred in classification problems, will also be used in this study. The aim of this study is to classify the reflow status, which is the target variable, using the XGBoost ML method and to identify the risk factors affecting reflow with the help of variable importance values.

The objective of this study is to bridge this gap in the literature. Specifically, the study aims to employ Explainable AI (XAI) methodologies to evaluate the predictive efficacy of these hematological parameters and the HALP score for the no-reflow in STEMI patients undergoing PPCI.

Material And Methods

Study Design and Data

This investigation adopts a retrospective observational design, encompassing a cohort of STEMI patients who underwent PPCI at our medical institution between January 2020 and September 2023. The cohort was subsequently dichotomized into two subsets based on the presence or absence of the no-reflow phenomenon, totaling 232 individuals.

Ethical Considerations

Ethical clearance for this study was duly obtained from the institutional ethics committee, ensuring that the research adheres to established ethical guidelines (Date: 20.09.2023; Protocol number: 2023/17/10).

Inclusion and Exclusion Criteria

The inclusion criteria for this study were meticulously predicated on the 2017 European Society of Cardiology (ESC) Guidelines for the management of AMI in patients presenting with STEMI (25-27). Exclusion criteria were delineated to mitigate potential confounding variables and included age restrictions, drug interactions affecting complete blood count, and pre-existing medical conditions such as renal impairment or a recent history of cancer.

a) Age >18 years and 80 years.

The exclusion criteria from the study are given follow as:

a) Age <18 years and >80 years,
b) Patients use drugs known to affect the complete blood count,
c) Patients with a hemoglobin value of less than 10 g/dl,
d) Patients with active bleeding,
e) Patients with severe renal impairment
f) A history of cancer was detected within the previous year,
g) Patients with severe liver impairment.

Data Collection

Data pertaining to demographic variables, MI locations, and comorbidities were extracted from electronic medical records. Hematological and biochemical parameters were ascertained from venous blood samples obtained during the initial emergency department admission. Age, gender, MI locations, and underlying diseases were obtained from the medical records of the patients and the control group at the first admission to the hospital. At the same time, the hematological and biochemical laboratory results from the venous blood taken at the first application to the emergency department gathered from the groups were; urea (mg/dL), creatinine, albumine (Alb), c-reactive protein (CRP), aspartate transaminase (AST), alkaline phosphatase (ALT), troponin (Tn), hemoglobin (Hbg) values, hematocrit (Hct) values, mean corpuscular volume (MCV) values, mean corpuscular hemoglobin (MCH) values, mean corpuscular hemoglobin concentration (MCHC) value, red-cell distribution width-standard deviation (RDW-SD) values, RDW-coefficient of variation (RDW-CV) values, mean platelet volume (MPV) values, platelet width of distribution (PDW) values, procalcitonin (PCT) values, platelet (PLT) counts and white blood cell (WBC), neutrophil (NEU), lymphocyte (LY), NLR, basophil (BA), monocytes (MO) and eosinophil (EO) counts.

HALP Score Calculation

The HALP score was computed using a standardized formula: Hemoglobin (g/L) × Albumin (g/L) × Lymphocytes (/L) / Platelets (/L), serving as a key variable in the study's predictive model.

Machine Learning -XGBoost

Gradient Boost is a useful machine learning strategy for regression and classification issues in which weak prediction models commonly yield decision tree ensembles. Gradient Boost, which is based on the boosting approach, tries to build several weak learners sequentially and integrate them into a complicated model (28).

Extreme Gradient Boosting (XGBoost) is a supervised learning approach that uses gradient boosting machines (GBM). Its foundation is built on gradient boosting and decision tree methods. When compared to other algorithms, it offers a substantial speed and performance advantage. XGBoost is also highly predictive, ten times quicker than other algorithms, and incorporates a number of regularizations that boost overall performance while decreasing overfitting and over-learning. XGBoost can improve performance by managing the complexity of the trees through the use of various regularization approaches (29,30).

Machine Learning Modeling and Performance Evaluation

In the study, variable selection was made in order to determine the most prominent features affecting the dependent variable in the data set. Random Forest variable selection method was used as the variable selection method. In the current study, XGBoost was utilized in the modeling stage for the dataset. As a training and test dataset, the data set was divided 80:20. The n-fold cross-validation approach was used in the analyses. The data is separated into n parts in the n-fold cross-validation procedure, and the model is applied to n parts. One of the n components is utilized for testing, while the remaining n-1 components are used to train the model. In this study, 5-fold cross-validation was employed for the modeling process. Accuracy, balanced accuracy, sensitivity, selectivity, positive predictive value, negative predictive value, and F1-score were used as performance evaluation criteria. In addition, variable importances were calculated, which gives information about how much the input variables attach importance to the output variable.

Biostatistical Analysis

The numerical variables in the dataset are summarized with median (95% confidence interval for median) and mean±standard deviation. while the qualitative variables are summarized with count (percentage). The conformity of the data to a normal distribution was checked with the Shapiro-Wilk test. Depending on the data distribution. independent sample t-test or Mann-Whitney U test was used for statistical analysis. A $p \leq 0.05$ was considered statistically significant. Analyses were performed using IBM SPSS Statistics 25.

Results

A total of 232 patients were retrospectively included in the study, of which 173 (78.88%) were patients with normal-reflow and 49 (21.12%) were patients with no-reflow between January 2020 and September 2023. Of the participants, 72 (31.0%) were female and 160 (69.0%) were male. Descriptive statistics of the quantitative variables in the current study are given in Table 1.

Descriptive statistics of the qualitative variables in the study are given in Table 2.

Table 1: Descriptive statistics for quantitative variables

Variable	Median (95% confidence interval)
Age (years)	60(60-63)
White Blood Cell ($10^{9/L}$)	11.6(11.2-12)
Hemoglobin (g/dL)	14.1(13.8-14.5)
Red Blood Cell ($10^{12/L}$)	4.82(4.78-4.91)
Basophil ($10^{9/L}$)	0.06(0.06-0.08)
Eosinophil ($10^{9/L}$)	0.115(0.1-0.14)
Lymphocyte ($10^{9/L}$)	2.605(2.49-2.87)
Monocyte ($10^{9/L}$)	0.735(0.7-0.8)
Neutrophil ($10^{9/L}$)	7.235(6.72-7.77)
Mean Platelet Volume (pg)	9.35(9.1-9.5)
Platelet ($10^{9/L}$)	267(258-278)
Hematocrit (HCT)	41.70(41-42.60)
MCV	87.05(86.1-87.9)
RDW-SD	41.3(40.4-42)
RDW-CV	13.6(13.6-13.9)
MCH (pg)	29.5(29.1-29.8)
MCHC (g/dL)	33.9(33.7-34.1)
PDW (fL)	16.2(15.9-16.39)
PCT (%)	0.24(0.24-0.26)
Albumin (g/dL)	41(41-42)
HALP score	5.906(5.477-6.354)
MPV/LY ratio	3.4(3.215-3.714)
NEU/LY ratio	2.581(2.196-2.938)
PLT/LY ratio	95.567(89.607-106.923)

WBC: leukocyte; RBC: erythrocyte; HGB: hemoglobin; BA: basophil; EO: eosinophil; LY: lymphocyte; MO: monocyte; NEU: neutrophil; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MPVLR: mean platelet volüme/lymphocyte ratio; LMR: lymphocyte/monocyte ratio; MPV: mean platelet volume; PLT: platelet; HCT: hematocrit; RDW-SD: red cell distribution width-standard deviation; RDW-CV: Red cell distribution width-coefficient of variation; MCH: mean erythrocyte hemoglobin; MCHC: mean corpuscular hemoglobin concentration; PDW: platelet distribution width; PCT: procalcitonin test.

Table 2: Descriptive statistics for qualitative variables

Variables	Categories	Count (%)
Reflow	NORMAL-REFLOW	183 (78.88)
	N0-REFLOW	49 (21.12)
Mi Location	Acute Inferior MI	135 (58.18)
	Acute Anterior MI	97 (41.82)
Gender	Female	72 (31.03)
	Male	160 (68.97)

Tablo 3: Statistical analysis results of normally distributed variables

Variables		REFLOW		*p*
		Normal-Reflow (N=183)	No-Reflow (N=49)	
		Mean±Standart Deviation		
Age (years)		59.858±9.8	58.939±11.4	0.577*
Variables	Categories	Count (%)		
MI Location	Acute inferior	104[a] (56.8)	31[b] (63.2)	0.063**
	Acute anterior	79 [a] (43.2)	18 [b] (36.8)	
Gender	Female	55 (30.1)	17 (34.7)	0.653**
	Male	128 (69.9)	32 (65.3)	

*: Independent sample t-test; **: Pearson chi-square test with Yates correction; myocardial infarction (MI); MI locations.

The results on whether there are statistical differences in demographic parameters in terms of the categories of the reflow variable are given in Table 3.

As a result of the analyses, no statistically significant difference was found between the categories of the reflow variable and the categories of the age variable, MI location variable, and gender variable. The results of whether there were statistical differences in the blood parameters in terms of the categories of the reflow variable are given in Table 4.

Tablo 4: Statistical analysis results of non-normally distributed variables

	REFLOW		*p*
Variables	**NORMAL-REFLOW(n=183)**	**NO-REFLOW(n=49)**	
	Median (95% confidence interval)		
White Blood Cell ($10^{9/L}$)	11.2(10.7-11.75)	13.5(12.2-14.35)	**<0.001***
Hemoglobin (g/dL)	14(13.6-14.5)	14.5(13.7-15.1)	0.521*
Basophil ($10^{9/L}$)	0.06(0.05-0.08)	0.07(0.05-0.1)	0.198*
Eosinophil ($10^{9/L}$)	0.11(0.1-0.15)	0.13(0.1-0.26)	0.801*
Lymphocyte ($10^{9/L}$)	2.6(2.48-2.89)	3.06(2.4-4.5)	0.060*
Monocyte ($10^{9/L}$)	0.7(0.7-0.79)	1(0.9-1.1)	**<0.001***
Neutrophil ($10^{9/L}$)	6.8(6.2-7.6)	8.69(8.11-9.36)	**0.001***
MPV (fL)	9.4(9.19-9.69)	9.3(8.5-9.8)	0.378*
Platelet ($10^{9/L}$)	265(252-275)	290(265-345)	**0.017***
MCV (fL)	87.3(86.6-88.3)	86.1(85-88.1)	0.282*
RDW-SD	41.2(40.3-42)	41.7(40-42.9)	0.700*
RDW-CV	13.5(13.4-13.7)	13.7(13.5-14.3)	0.124*
MCH (pg)	29.6(29.1-30.1)	29.5(28.3-30)	0.230*
MCHC (g/dL)	34(33.9-34.2)	33.7(33.5-34.2)	0.804*
PDW (fL)	16.2(15.8-16.39)	16.3(15.9-16.8)	0.346*
PCT (%)	0.24(0.24-0.26)	0.26(0.25-0.3)	0.059*
Albumin (g/dL)	41.3(41-42)	40(38-42)	**0.031***
HALP score	5.794(5.318-6.252)	6.464(5.338-8.409)	0.437*
MPV/LY ratio	3.511(3.269-3.855)	3.2(2.042-4.038)	**0.041***
NEU/LY ratio	2.445(2.168-2.85)	3.055(2.031-3.908)	0.667*
PLT/LY ratio	98(91.111-108.772)	85.946(73.786-112.162)	0.272*
	Mean ± Standard Deviation		
Red Blood Cell ($10^{12/L}$)	4.794±0.579	4.864±0.68	0.469**
Hematocrit (%)	41.384±4.629	41.598±5.185	0.779**

*:Mann Whitney U test, **:Independent sample t test, WBC: leukocyte; RBC: erythrocyte; HGB: hemoglobin; BA: basophil; EO: eosinophil; LY: lymphocyte; MO: monocyte; NEU: neutrophil; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MPVLR: mean platelet volüme/lymphocyte ratio; MPV: mean platelet volume; PLT: platelet; HCT: hematocrit; RDW-SD: red cell distribution width-standard deviation; RDW-CV: Red cell distribution width-coefficient of variation; MCH: mean erythrocyte hemoglobin; MCHC: mean corpuscular hemoglobin concentration; PDW: platelet distribution width; PCT: procalcitonin test; HALP score (Hemaglobin*Albumin* Lymphocyte/Platelet).

As a result of the analyses, a statistically significant difference was observed in white blood cell (WBC), monocyte (MO), neutrophil (NEU), platelet (PLT), albumin, and MPV/LY variables in terms of the categories

of the reflow variable ($p<0.05$). For the other variables. no statistically significant difference was found in terms of the categories of the reflow variable.

The results of the performance metrics obtained for the test and training data as a result of modeling with XGBoost for the remaining variables and the reflow variable after the variable selection are given in Table 5.

Table 5: Results for performance metrics obtained from the XGBoost model

Metric	Training set Value	Test set Value
Accuracy	86.1	84.4
Balanced Accuracy	70.2	61.1
Sensitivity	42.5	22.2
Specificity	98	100
PPV	85	100
NPV	86.2	83.7
F1 score	56.7	36.4

In the training stage accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score obtained from the random forest model were 86.1%, 70.2%, 42.5%, 98%, 85%, 86.2%, and 56.7%, respectively. Also in the testing stage accuracy, balanced accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score obtained from the RF model were 84.4%, 61.1%, 22.2%, 100%, 100%, 83.7%, and 36.4%, respectively. Performance metrics are plotted for the XGBoost model in Figure 1.

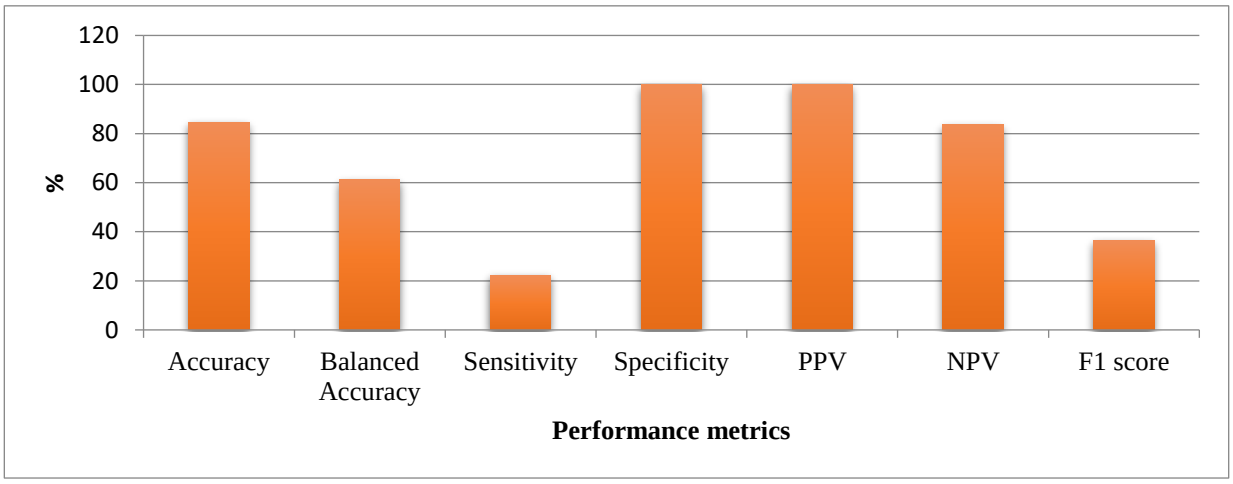


Figure 1: Graph of performance metrics

The graph of the variables associated with the output variable according to the variable importance obtained from the modeling is given in Figure 2.

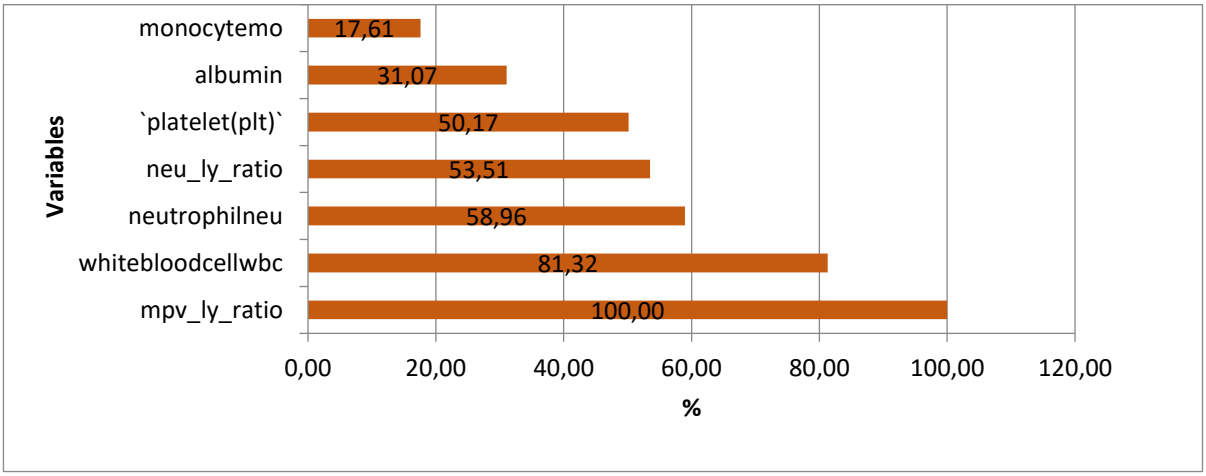


Figure 2: Variable importance graph

Discussion

The study presents a comprehensive analysis of both quantitative and qualitative variables related to blood parameters, demographic characteristics, and clinical outcomes. Descriptive statistics provide a snapshot of the central tendencies and variability within the dataset, while inferential statistics offer insights into the relationships between variables, particularly in terms of the 'reflow' categories.

In terms of blood parameters, significant differences were observed in white blood cell count (WBC), monocyte (MO), neutrophil (NEU), platelet (PLT), albumin, and the MPV/LY ratio when comparing the 'NORMAL-REFLOW' and 'NO-REFLOW' categories. These findings indicate that these specific blood parameters could serve as potential biomarkers for predicting reflow outcomes.

The XGBoost model demonstrated good performance in the training set with an accuracy of 86.1%, balanced accuracy of 70.2%, and an F1 score of 56.7%. However, the model's performance slightly declined in the test set, particularly in terms of balanced accuracy and sensitivity, which dropped to 61.1% and 22.2%, respectively. Despite the high specificity and positive predictive value (PPV) in both training and test sets, the low sensitivity in the test set suggests that the model may not be as effective in identifying 'NO-REFLOW' cases, which could be a limitation.

In comparison, the Random Forest (RF) model also showed a similar trend, with high accuracy but lower sensitivity and F1 score in the test set. This indicates that while the model is good at making correct predictions overall, it may struggle with identifying the less prevalent class in the dataset.

The study's findings have several clinical implications. The identification of specific blood parameters as potential biomarkers can guide clinicians in risk stratification and decision-making. However, the lower sensitivity in the test set suggests that the model may benefit from further tuning or the inclusion of additional features to improve its predictive power for 'NO-REFLOW' cases.

Future research could focus on incorporating more features or employing different machine learning algorithms to improve model performance. Additionally, external validation with a larger and more diverse dataset could provide more generalizable results.

This study used biostatistical analysis and XAI to investigate potential hematological indicators for predicting no-reflow. The observed results indicated that the WBC, MO, NEU, and PLT values of patients with no flow were statistically higher than those of the patients with normal flow (p<0.05). However, compared to patients with normal-flow, patients with no-reflow had significantly reduced albumin, and MPVLR levels (p<0.05). However, the HALP score was found to be statistically insignificant in both groups. In this study, according to artificial intelligence analysis, MPVLR, WBC, and NEU were most important hematological parameter in predicting no-relow.

A series of pathophysiological events occur in AMI that produce an intense inflammatory response mediated by myocardial ischemia. Neutrophils, white blood cells first detected at the infarct site due to oxidative stress. This is followed by white blood cells monocytes and lymphocytes, which then phagocytize the necrotic remnants by releasing proteo-enzymes and cytokines. In addition, activated platelets interact with neutrophils, monocytes, and lymphocytes, both acutely accelerating coronary artery occlusion and enhancing the inflammatory response. Previous studies have shown that the stronger this inflammatory response, the more severe the vascular thrombogenic state and the increased development of coronary no-reflow in invasive percutaneous coronary procedures, resulting in a worse prognosis in acute myocardial infarction (31-34). In our current study, according to the descriptive statistics results; WBC, NEU, and MO counts were found to be significantly higher in patients with no reflow than in patients with normal reflow (p<0.05). Similarly, artificial intelligence analysis; WBC, and NEU were some of the most important hematological parameters to predict no-reflow. The reason why the WBC and NEU numbers were higher in the no-reflow group compared to the normal-reflow group may be due to the more severe inflammatory response of myocardial ischemia in STEMI patients. As a result, this can lead to a poor AMI prognosis.

Recent studies have shed light on the prognostic utility of specific hematological indices, such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume-to-Lymphocyte Ratio (MPVLR), in predicting adverse outcomes in STEMI patients (14-18). In another study, MPVLR was found to be moderately effective in demonstrating the no-relow (35). In this study, according to artificial intelligence analysis, the most important hematological parameter in predicting no-relow was MPVLR.

Previous studies have shown that high-sensitivity C-reactive protein (hs-CRP), neutrophil count, lymphocyte count, monocyte count, and albumin are important inflammatory markers in the inflammatory process of atherosclerosis, plaque development, and plaque progression (36,37). Adverse cardiovascular outcomes and the prevalence of atherosclerosis are significantly associated with high CRP levels (38). Additionally, another

study has shown that CRP/albumin ratio (CAR) is an important biochemical marker for predicting no reflow (39). In our study, albumin level was significantly lower in the non-reflow group. A study found that coronary artery disease and heart failure were more common in men, and rheumatic mitral valve disease and Takotsubo cardiomyopathy were more common in women (40). However, in the current study, the gender factor between the no-reflow and normal-reflow groups were statistically similar in both groups.

Limitations

The study has some limitations. First, the number of patients in the study limited. Second, our data source included patients from only 1 geographic region of Turkey, which limits generalizability and requires validation in other populations.

Conclusions

In our study, according to artificial intelligence analysis, the most important hematological parameter in predicting no-reflow was MPVLR. However, in this study, HALP score was not found to be effective in predicting no-reflow. The study offers valuable insights into the factors affecting reflow outcomes in patients, with specific blood parameters showing promise as predictive biomarkers. While the machine learning models employed show good predictive accuracy, there is room for improvement, particularly in enhancing the sensitivity of the models. Further research is needed to validate these findings and improve the predictive models.

Acknowledgements: none

Ethical Approval: *The study protocol was approved by the Samsun University Clinical Trials and Ethics Committee no: 2023/17/10*

Author Contributions: *Concept: RY, Literature Review: RY Design: RY Data acquisition: RY Analysis and interpretation: RY Writing manuscript: RY Critical revision of manuscript: RY*

Conflict of Interest: *The author(s) do not have any potential conflict of interest regarding the research, authorship and/or publication of this article.*

Financial Disclosure: *This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.*

References

1.Nascimento BR, Brant LCC, Marino BCA, et al. Implementing myocardial infarction systems of care in low/middle-income countries. Heart. 2019 ;105(1):20-6.
2.Barberi C, van den Hondel KE. The use of cardiac troponin T (cTnT) in the postmortem diagnosis of acute myocardial infarction and sudden cardiac death: A systematic review. Forensic Sci Int. 2018 ; 292:27-38.
3.Alaour B, Liew F, Kaier TE. Cardiac Troponin - diagnostic problems and impact on cardiovascular disease. Ann Med. 2018;50(8):655-5.
4.Haig C, Carrick D, Carberry J, et al. Current Smoking and Prognosis After Acute ST-Segment Elevation Myocardial Infarction:nNew Pathophysiological Insights. JACC Cardiovasc Imaging. 2019 ;12(6):993-1003.
5.Ito H. No-reflow phenomenon and prognosis in patients with acute myocardial infarction. Nat Clin Pract Cardiovasc Med. 2006;3(9):499-506.
6. Morishima I, Sone T, Okumura K, et al. Angiographic no-reflow phenomenon as a predictor of adverse long-term outcome in patients treated with percutaneous transluminal coronary angio- plasty for first acute myocardial infarction. J Am Coll Cardiol. 2000;36(4):1202-09.
7.Brosh D, Assali AR, Mager A, et al. Effect of no-reflow during primary percutaneous coronary intervention for acute myocardial infarction on six-month mortality. Am J Cardiol. 2007;99(4):442-5.
8.Durante A, Camici PG. Novel insights into an “old” phenomenon: the no reflow. Int J Cardiol 2015;187:273–80.
9.Tranum-Jensen J, Janse MJ, Fiolet WT, et al. Tissue osmolality, cell swelling, and reperfusion in acute regional myocardial ischemia in the isolated porcine. Circ Res 1981;49:364–81.
10. Reffelmann T, Kloner RA. The no-reflow phenomenon: A basic mechanism of myocardial ischemia and reperfusion. Basic Res Cardiol 2006;101:359 –72.
11. Bolli R, Jeroudi MO, Patel BS, et al. Direct evidence that oxygen- derived free radicals contribute to postischemic myocardial dysfunction in the intact dog. Proc Natl Acad Sci USA 1989;86:4695-9.
12. Ambrosio G, Tritto I. Reperfusion injury: Experimental evidence and clinical implications. Am Heart J 1999;138:S69 –75.
13. Skyschally A, Leineweber K, Gres P, et al. Coronary microembolization. Basic Res Cardiol 2006;101:373– 82.
14. Azab B, Shah N, Akerman M, et al. Value of platelet/ lymphocyte ratio as a predictor of all-cause mortality after non- ST-elevation myocardial infarction. J Thromb Thrombolysis. 2012;34(3):326-34.
15. Gursoy OM, Karakoyun S, Kalc ¸ik M, et al. Usefulness of novel hematologic inflammatory parameters to predict prosthetic mitral valve. Am J Cardiol. 2014;113(5):860-4.
16. Hudzik B, Szkodzin´ski J, Lekston A, et al. Mean platelet volume-to-lymphocyte ratio: a novel marker of poor short- and long-term prognosis in patients with diabetes mellitus and acute myocardial infarction. J Diabetes Complications. 2016;30(6):1097-02.

17. Akpek M, Kaya MG, Lam YY, et al. Relation of neutrophil/lym- phocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. Am J Cardiol. 2012; 110(5):621-627.
18. Kurtul A, Murat SN, Yarlioglues M, et al. Increased neutrophil- to-lymphocyte ratio predicts persistent coronary no-flow after wire insertion in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Clinics (Sao Paulo). 2015;70(1):34-40.
19. Guo Y, Shi D, Zhang J, et al. The hemoglobin, albumin, lymphocyte, and platelet (Halp) score is a novel significant prognostic factor for patients with metastatic prostate cancer undergoing cytoreductive radical prostatectomy. J Cancer 2019;10(1):81–91.
20. Peng D, Zhang C, Tang Q, et al. Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (Halp) in patients with renal cell carcinoma after nephrectomy. BMC Urol 2018;18(1):20.
21. Chen X, Xue L, Wang W, et al.Prognosticsignificance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: a retrospective cohort study. Oncotarget 2015;6(38):41370–82.
22. Tian M, Li Y, Wang X, et al. The hemoglobin, albumin, lymphocyte, and platelet (Halp) score is associated with poor outcome of acute ischemic stroke. Front Neurol 2020;11:610318.
23. Polikar R. Ensemble learning. Ensemble machine learning. Springer, Boston, MA; 2012:1-34.
24. Akman M, Genç Y, Ankarali H. [Random Forests Methods and an Application in Health Science]. Turkiye Klinikleri J Biostat. 2011;3(1):36.
25. Thygesen K, Alpert JS, Jaffe AS, et al. Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, ESC Committee for Practice Guidelines. Third universal definition of myocardial infarction. Eur Heart J 2012;33(20):2551–67.
26. Roffi M, Patrono C, Collet JP, et al. ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016;37:267315.
27. Ibanez B, James S, Agewall S, et al. ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018;39:119177.
28. Wang J, Li P, Ran R, et all. A short-term photovoltaic power prediction model based on the gradient boost decision tree. Appl Sci. 2018;8(5):689.
29. Dikker J. Boosted tree learning for balanced item recommendation in online retail. 2017.
30. Salam Patrous Z. Evaluating XGBoost for user classification by using behavioral features extracted from smartphone sensors. Computer Science. Master. KTH Royal Institute of Technology; 2018.
31. C. Chen, B. L. Cong, M. Wang, et al., "Neutrophil to lymphocyte ratio as a predictor of myocardial damage and cardiac dysfunction in acute coronary syndrome patients," Integrative medicine research, 2018;7:192-9.
32. A. Somaschini, S. Cornara, A. Demarchi, et al., "Neutrophil to platelet ratio: A novel prognostic biomarker in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention," European Journal of Preventive Cardiology, 2020;27:2338-40.
33. W. Li, Q. Liu, and Y. Tang, "Platelet to lymphocyte ratio in the prediction of adverse outcomes after acute coronary syndrome: a meta-analysis," Scientific reports, 2017; 7:40426.
34. H. Li, Y. Zhou, Y. Ma, et al. "The prognostic value of the platelet-to-lymphocyte ratio in acute coronary syndrome: a systematic review and meta-analysis," Kardiologia Polska (Polish Heart Journal), 2017;75:666-73.
35. Z. Wang, L. Ren, N. Liu, et al. Utility of Hematological Parameters in Predicting No-Reflow Phenomenon After Primary Percutaneous Coronary Intervention in Patients With ST-Segment Elevation Myocardial Infarction. Clinical and Applied Thrombosis/Hemostasis, 2018;24(7):1177-83.
36. Hosseinsabet A, Mohebbi A, Almasi A. C-reactive protein and Coronary Calcium Score association in coronary artery disease. Cardiol J. 2008;15:431–6.
37. Duffy BK, Gurm HS, Rajagopal V, Gupta R, Ellis SG, Bhatt DL. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol. 2006;97:993–6.
38. Redberg RF, Rifai N, Gee L, Ridker PM. Lack of association of C-reactive protein and coronary calcium by electron beam computed tomography in postmenopausal women: Implications for coronary artery disease screening. J Am Coll Cardiol. 2000;36:39–43.
39. Yucel K, Hatice Eftal SK, Idris Y, et al. CRP Albumin Ratio May Predict No Reflow in Patients Undergoing Percutaneous Coronary Intervention for Saphenous Vein Graft Stenosis. Angiology, 2023;74(1):55-61.
40. Usalp, S. The Role of Gender in Heart Diseases. International Journal of Current Medical and Biological Sciences, 2021;1(1):1-6.

IJCMBS

THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Orgınal Article

Tissue Oxygenation Change on Upper Extremities After Ultrasound-Guided Axillary Brachial Plexus Blockade; Prospective Observational Study

Ultrason Kılavuzluğunda Aksiller Brakial Pleksus Blokajı Sonrası Üst Ekstremitelerde Doku Oksijenasyonu Değişimi; Prospektif Gözlemsel Çalışma

Maruf Sürücü[1*], Mahmut Alp Karahan[1], Şaban Yalçın[2], Nuray Altay[3], Evren Büyükfırat[3], Aytekin Yeşilay[3]

[1]Department of Anesthesiology and Reanimation, University of Health Science, Mehmet Akif İnan Training and Search Hospital, Şanliurfa, Turkiye,

[2]Kayseri Training and Research Hospital, Intensive Care, Kayseri, Turkiye

[3]Department of Anaesthesiology and Reanimation, Harran University, Faculty of Medicine, Sanliurfa, Turkiye

**Corresponding author:*

Dr. Maruf Sürücü , MD

Adress:University of Health Science Turkey, Mehmet Akif İnan Training and Search Hospital Haliliye, 63000, Sanliurfa , Turkiye.

E-mail:msurucu1986@gmail.com

Received:12/07/2023

Accepted:12/09/2023

Cite as:SURUCU. M. and et al. Tissue Oxygenation Change on Upper Extremities After Ultrasound-Guided Axillary Brachial Plexus Blockade; Prospective Observational Study. IJCMBS 2023;3(3):156-61 doi.org/10.5281/zenodo.10047189

Highlights

•The Tissue oxygen saturation increases after peripheral plexus blockade and may be used as an indicator for successful block placement in awake patient.

• Tissue oxygen saturation monitoring may provide a highly valuable tool to quickly evaluate the success of regional anesthesia of the upper extremity in clinical practice.

Abstract

Background: The aim of the study was to investigate whether tissue oxygen saturation (St02) using the Near Infrared Spectroscopy method (NIRS), is a reliable and objective method for assessing the adequacy of axillary blockade and to describe the time course of StO2 changes.

Materials and Methods

The study was approved by the Ethical Committee and met the Declaration of Helsinki criteria. In this prospective observational study, St02 was measured in 30 patients scheduled for elective hand surgery under axillary nevre block. Non-invasive StO2 -monitoring (InSpectra™ StO2, Hutchinson Technology Inc., Hutchinson, Minnesota, USA) was used in patients before ultrasound guided axillary brachial plexus blockade and during the first 30 minute of the blockade.

Results

StO2 measurements were statistically increased in 1st ,5th, 10th, 15th, 20th, 25th, 30th minutes compared to baseline levels ($p< 0.05$ for all comparisons). Mean StO2 levels of the hand with axillary brachial plexus blockade were statistically increased compared the levels of the hand StO2 without blockade in 15th, 20th, 25th, 30th. minutes ($p< 0.05$ for all comparisons).

Conclusion

There has been found a significant correlation between tissue StO2 values of two limbs using NIRS in axillary blockage operations of upper extremity.

Keywords: Brachial plexus, Axillary block, Near Infrared Spectroscopy, Tissue oxygenation, Regional anesthesia

ÖZ

Amaç: Near-infrared Spektroskopi (NIRS) yöntemi kullanılarak doku oksijen satürasyonunun (St02), aksiller blokajın yeterliliğini değerlendirmede güvenilir ve objektif bir yöntem olup olmadığını ve StO2 nin zaman içindeki değişikliklerinin tespit etmektir. **Gereç ve Yöntem** Harran Üniversitesi Araştırma ve Uygulama Hastanesi Etik Kurul ve hastaların onayı alındıktan sonra aksiler bolk uygulanan elektif el cerrahisi planlanan 30 hastada St02 ölçüldü. Non-invaziv StO2 takibi (InSpectra™ StO2, Hutchinson TechnologyInc., Hutchinson, Minnesota, ABD), hastalarda ultrason kılavuzluğunda aksiller brakiyal pleksus blokajı öncesinde ve blokajın ilk 30 dakikasında kullanıldı.

Bulgular: StO2 ölçümleri 1.,5., 10., 15.,20.,25.,30. dakikalarda başlangıca göre istatistiksel olarak arttı (tüm karşılaştırmalar için $p< 0.05$). Aksiller brakiyal pleksus blokajı yapılan elin ortalama StO2 seviyeleri blokaj yapılmayan elin StO2 seviyelerine göre 15.,20., 25., 30. dakikalarda istatistiksel olarak yüksek bulundu. (tüm karşılaştırmalar için $p< 0.05$). **Sonuç:**Üst ekstremite operasyonlarında uygulanan aksiller blokajda NIRS kullanılarak iki ekstremite StO2 değerleri arasında anlamlı bir ilişki bulunmuştur.

Anahtar Kelimeler: Brakiyal pleksus, Aksiller blok, Near İnfrared Spekstroskopisi, Doku oksijenizasyonu, Rejyonal anestezi

Introduction

A peripheral nerve block is one of the blocks commonly used in regional anesthesia. In cases where general anesthesia poses risks, such as in heart, kidney, respiratory system diseases, chest trauma, and diabetic patients, peripheral nerve blocks provide more advantageous conditions (1). The brachial plexus block, which is one of the most frequently used peripheral nerve blocks, can be used in surgical procedures and pain management involving the upper extremities. The block is limited to the region innervated by the plexus or its terminal branches, while the rest of the body remains under physiological control (2). Axillary block is a technique in which the brachial plexus is blocked in the axillary area. The brachial plexus nerves, along with the axillary artery, are located in an easily accessible position in the axilla. Due to its anatomical structure, it is more reliable and easily accessible, which makes it more easily accepted by the patient. Axillary brachial plexus block has fewer side effects, is easy to perform with ultrasound, and has a high success rate (3).

The measurement of the success of peripheral nerve blocks is a subject of discussion and generally relies on patient-based traditional methods. However, multi-purpose techniques have been discussed in recent literature for the success of peripheral nerve blocks. These techniques include perfusion index (PI), plethysmographic variability index (PVI), non-invasive tissue hemoglobin monitoring (SpHb), tissue oxygen saturation (StO2), tissue hemoglobin index (THI), and body temperature (4-8).

Near-Infrared Spectroscopy (NIRS) is a technique that non-invasively measures the oxygenation of biological tissues such as muscle tissue, providing relatively low-cost information. It works based on the principle that near-infrared light at different wavelengths (680–800 nm) is absorbed to varying degrees by oxygenated and deoxygenated hemoglobin molecules in the measured area, and the ratio of oxygenated hemoglobin to total hemoglobin is expressed as a percentage. It provides local oxygen saturation during measurement. It is analyzed to determine the ratio of oxygenated hemoglobin to total hemoglobin and expressed as a percentage, known as StO2 (6).

We defined our hypothesis as the local effects generated by successful upper extremity peripheral nerve blocks leading to detectable increases in tissue oxygen saturation levels measured by the NIRS method. In line with our hypothesis, we aimed to determine whether the changes observed with axillary block using the NIRS method affect microcirculation and tissue oxygen saturation and also investigate whether NIRS is a reliable and objective method for assessing the adequacy of peripheral nerve blocks.

Material and Method

A total of 30 patients between the ages of 18 and 65, classified as ASA (American Society of Anesthesiologists) I-II, who were scheduled for hand, forearm, and arm surgery, were included in our hospital's study. Patients who did not want to participate in the study, those for whom axillary block was contraindicated, those who were unable to cooperate, those with renal or liver failure, pregnant and lactating women, anemic patients and patients classified as ASA III-IV-V were excluded from the study. Anesthetic procedures were performed by the same anesthesiologist. Starting at midnight before the operation, all patients were instructed to refrain from oral intake, and a balanced electrolyte solution (Isolyte®) was initiated at a rate of 2 ml/kg/hour. Sedation was not administered to the patients on the morning of the surgery. Prior to the procedure, an 18-20 G intravenous catheter was inserted into the dorsum of the hand or antecubital region of each patient, and volume replacement was performed with 10 ml/kg of 0.9% isotonic NaCl solution. Standard monitoring (ECG, SpO2, and non-invasive arterial blood pressure) was performed. Baseline systolic arterial blood pressure (SAB) and heart rate (HR) were recorded. NIRS probes were placed on the palm (thenar region) of both the upper extremity to be blocked and the other extremity (thenar region), and baseline StO2 was recorded. The arm was positioned in 90 degrees of abduction for the axillary region and in a position creating a 90-degree angle with the arm for the forearm. After necessary sterilization procedures were performed in the axillary region and the block site was covered with sterile drapes, axillary artery palpation was performed. Using a portable ultrasound device (MyLab™Sat portable ultrasound, Italy) with a frequency range of 2–18 MHz (MyLab™Sat Linear Probe, Italy), a 4 cm linear ultrasound probe was placed above and below the palpated area in contact with a neurostimulator (StimuplexDig®, B. Braun, Germany) attached to a 22G 50 mm electrically insulated needle (Stimuplex®, B. Braun, Germany). The in-plane technique was used to inject equal volumes (10 ml) of the prepared solution around each nerve after providing a motor response of 0.2-0.5 mA electrical stimulation to the terminal branches of the brachial plexus (median, ulnar, radial, and musculocutaneous) and observing sufficient muscle contraction following the aspiration test. For the block, a total of 40 ml of local anesthetic (LA) solution was prepared, consisting of 24 ml of 0.5% bupivacaine and 16 ml of 0.9% saline solution. All patients received a total of 40 ml (24 ml of bupivacaine and 16 ml of 0.9% saline) from the prepared solution.

After the completion of the axillary block, sensory and motor blocks were evaluated every 5 minutes within the first 30 minutes. Additionally, SpO2, heart rate, non-invasive arterial blood pressure, and StO2 were recorded every 5 minutes. The block onset time was considered to be 30 minutes. At the 30-minute mark, sensory block level was evaluated using the pinprick test, and motor block degree was assessed using the Bromage scale. Subsequently, patients were allowed to proceed with their surgical procedures.

Statistical Analysis

The numerical data obtained in the study were expressed as mean ± standard deviation, while categorical data were presented as percentages and frequencies. SPSS Version 24 software was used for statistical analysis. Compliance of numerical data to normal distribution was tested with Shapiro–Wilk test. Furthermore, the Wilcoxon test was used to compare the non-normally distributed variables between the block group and the control group, while the Freidman test was used to compare the measurements obtained at different times (intragroup comparison).The data were presented in tables as mean and standard deviation, with a significance level of 0.05.

Results

A total of 30 individuals were included in the study, of whom 19 (63.33%) were female and 11 (36.66%) were male (Table 1). Meanagewas 42.5 ± 11.53 years. In all patients, it was determined that the performed nerve block was effective for intraoperative anesthesia or postoperative analgesia, and no patient suffered from pain after surgery.

Table-1. Demographic Data of Our Study

Varaibles	n: 30
Age (year), mean	42.5(14.04)
Gender	
Male (%)	11 (36.7)
Female (%)	19 (63.3)
ASA	
I (%)	12 (40)
II (%)	18 (60)
Additional disease	
No (%)	12 (40)
Yes n(%)	18 (60)

A significant decrease was found in heart rate measured at different time points compared to the baseline **(Figure 1).** When comparing systolic blood pressure measured at different time points, significant decreases were observed at 1 minute (p = 0.027), 5 minutes (p=0.012), 10 minutes (p=0.011), and 15 minutes (p= 0.05) compared to the baseline measurements, while there was no significant difference between the other time points [20 minutes (p= 0.229), 25 minutes (p= 0.333), and 30 minutes (p= 0.259)]. When comparing diastolic blood pressure measured at different time points, significant decreases were found at 1 minute (p=0.004), 5 minutes (p= 0.003), and 10 minutes (p=0.009) compared to the baseline measurements, while there was no significant difference between the other time points [15 minutes (p=0.136), 20 minutes (p=0.084), 25 minutes (p=0.421), and 30 minutes (p=0.118)] in diastolic blood pressure measurements.

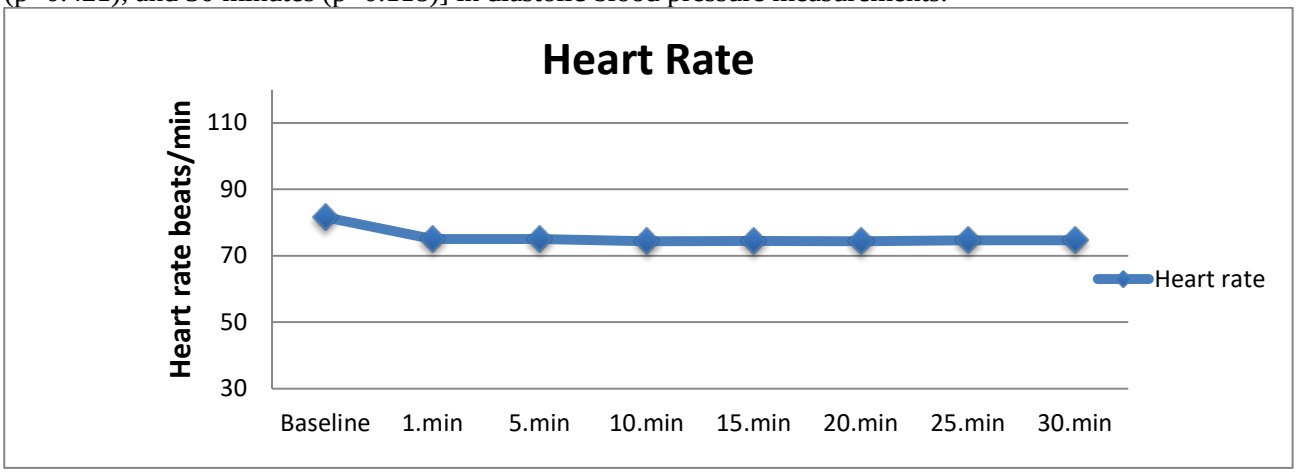
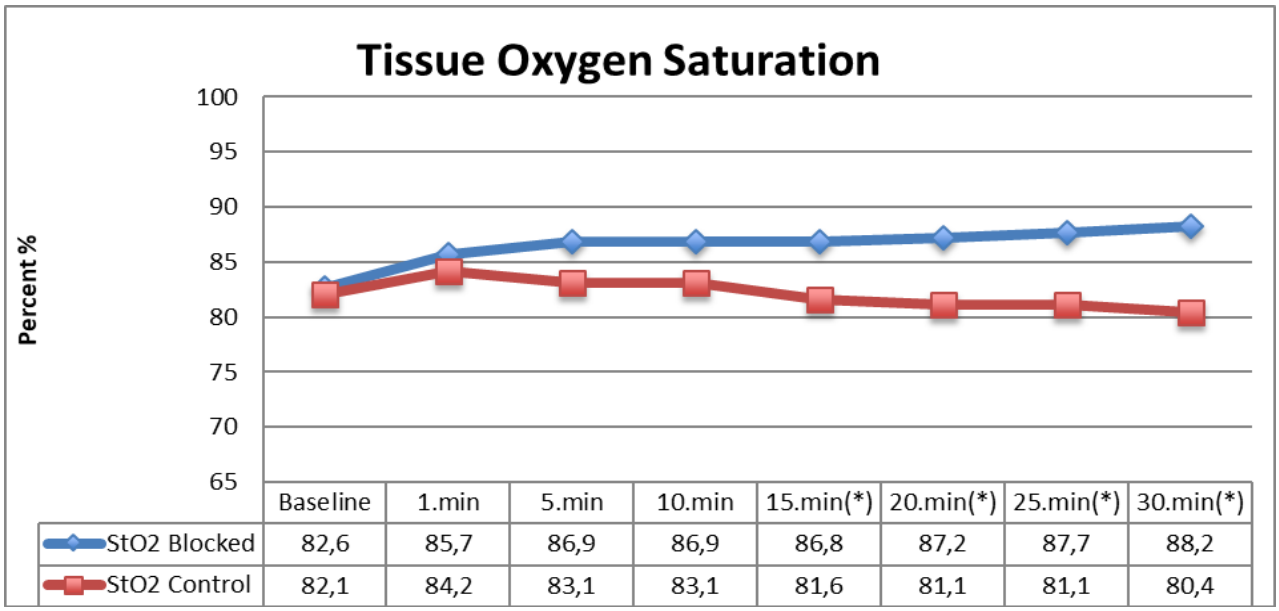


Figure 1: Average Values of Peak Heart Rate

When comparing the StO2 levels measured at different time points (1 minute, 5 minutes, 10 minutes, 15 minutes, 20 minutes, 25 minutes, and 30 minutes) on the side where axillary block was not performed, no significant difference was found compared to the baseline values (p=0.151, p=0.171, p= 0.42, p= 0.151, p= 0.511, p= 0.215, p= 0.093).
When comparing the StO2 levels measured at different time points (1 minute, 5 minutes, 10 minutes, 15 minutes, 20 minutes, 25 minutes, and 30 minutes) on the side where axillary block was performed, significant differences were found at 15 minutes (p=0.005), 20 minutes (p=0.003), 25 minutes (p=0.001), and 30 minutes (p= 0.001) compared to the baseline values and compared to the contralateral non-blocked side. The StO2 values measured at those time points were significantly higher. Statistically, the mean StO2 values on the blocked side were significantly higher than the contralateral side at 15 minutes, 20 minutes, 25 minutes, and 30 minutes ($p < 0.05$) .

Changes in Tissue Oxygenation After Peripheral Nerve Block

Statistically, the mean StO2 values were significantly higher on the blocked side compared to the contralateral side at 15 minutes, 20 minutes, 25 minutes, and 30 minutes ($p < 0.05$). The mean StO2 value on the blocked side was 85.7 at 1 minute, while it was 84.2 on the other arm. At 30 minutes, the mean StO2 value on the blocked side increased to 88.2, whereas it was 80.4 on the other arm **(Figure 2).** No complications or adverse effects were observed in our study.



	Baseline	1.min	5.min	10.min	15.min(*)	20.min(*)	25.min(*)	30.min(*)
StO2 Blocked	82,6	85,7	86,9	86,9	86,8	87,2	87,7	88,2
StO2 Control	82,1	84,2	83,1	83,1	81,6	81,1	81,1	80,4

(*): The mean StO2 values were significantly higher on the blocked side at the indicated minutes ($p < 0.05$).

Figure 2: StO2 Values in Blocked and Non-Blocked Arms

Discussion

The aim of our study was to evaluate the effects of changes induced by axillary block on microcirculation and tissue oxygen saturation using the NIRS method and to measure the success of the block. In our study, in the extremity where the axillary block was performed, the tissue oxygen saturation value measured at 15,20,25 and 30.minutes was found to be significantly higher compared to the baseline and the non-blocked extremity.
Regional anesthesia is a commonly preferred anesthesia technique in upper extremity surgery due to its many advantages. These advantages, such as minimal analgesic and antiemetic consumption, shorter recovery room and hospital stays, facilitated pain control transition, increased blood flow in the extremity, theoretically lower frequency of reflex sympathetic dystrophy, less urinary retention, and no need for tracheal intubation (9).
The fundamental requirement for a successful block in regional anesthesia is the proper application of the LA around the nerve tissue. (10, 11).Successful peripheral nerve blockade results in local vasodilation, increased local blood flow, and some increase in skin temperature due to sympathetic fiber blocking.Since it can be used to evaluate arterial vasodilation caused by sympathetic blockade after peripheral nerve block, as well as to measure the increase in blood, this method may be the primary method of choice to evaluate flow rate and block efficiency. At this point, numerical values such as StO2, PI, and PVI become important for objectively measuring block success. Assessing block success in a more objective manner prevents unnecessary opioid

administration and unnecessary general anesthesia. This will ensure that surgical durations do not unnecessarily extend and that additional costs are not incurred. NIRS reflects changes in vasomotor tone that vary between patients; therefore, block adequacy can only be assessed by determining the NIRS rate of increase from baseline (12).

There are not many studies in the literature regarding the use of NIRS in the field of regional anesthesia. Okano et al. (13) investigated the effects of NIRS on the success of stellate ganglion block. They concluded that NIRS had successfully confirmed the stellate ganglion block.

Tsai et al. performed brachial plexus blocks (interscalene, supraclavicular, infraclavicular, and axillary) in 15 patients undergoing elective upper extremity orthopedic surgery and examined regional oxygen saturations in both extremities (operated extremity and healthy extremity). Although there was no difference at baseline, approximately 15% increases in oxygen saturation were observed in the blocked extremity starting in the 5th minute, and these increases were considered statistically significant (14).

Tighe et al. conducted a similar study to Tsai et al. They performed peripheral nerve blocks (cervical paravertebral nerve block, femoral nerve block, infraclavicular nerve block, and sciatic nerve block) in 40 elective patients undergoing surgery on the extremity and attempted to measure their effectiveness and differences compared to the other extremity using the NIRS method at 5-minute intervals. The initial StO2 values were found to be high in both extremities, and as the block became effective, the values started to increase (15).

Tsai et al. applied interscalene, supraclavicular, infraclavicular, and axillary block techniques for brachial plexus blocks (14). The LA they used and the dosage administered showed similarities to our study. Tighe et al., on the other hand, performed upper and lower extremity plexus blocks (cervical paravertebral nerve block, femoral nerve block, infraclavicular nerve block, sciatic nerve block) (15). Multiple LA were used in different doses. In our study, we applied a single type of block compared to the two studies conducted on the effectiveness of peripheral nerve blocks. Our results show similarities to those of Tsai et al.

Karahan et al. conducted a prospective observational study in which StO2 measurements were performed in 40 patients scheduled for elective hand surgery under infraclavicular block. StO2 measurements were taken before and during the first 30 minutes of the infraclavicular brachial plexus block under ultrasound guidance. Median StO2 values significantly increased by 4.5% at 5 minutes, 5.5% at 30 minutes, and an average of 1% between 5 and 30 minutes compared to the baseline values on the blocked side (16).

In the study by Topcam et al., the effects of local infiltrative anesthesia and supraclavicular brachial plexus block on tissue oxygenation and fistula patency were investigated in arteriovenous fistula surgeries. The patients undergoing arteriovenous fistula surgery were divided into two groups. Group L (n = 30) received local infiltrative anesthesia, while group B (n=30) received supraclavicular brachial plexus block. NIRS measurements of the patients were evaluated from the thenar region of both hands. One month after the surgery, Tissue oxygenation measured by NIRS monitoring in arteriovenous fistula surgery was found to be higher in the extremity where brachial plexus block was applied (17).In our studyTissue oxygenation of the upper extremities with and without axillary block was evaluated using NIRS; StO2 was found to be higher in the arm where the block was performed compared to the baseline value and the non-blocked side .

Study limitations

Our study was limited in two ways. First, our study was not a randomized and placebo-controlled study. Instead, the other extremity that did not undergo surgery was used as a control.The volume of the LA solution was quite high. A total of 40 mL of LA solution, 10 ml for each nerve, which is commonly used as a standard dose in our hospital, was applied to the blocked area. In extremity peripheral nerve blocks, administration of low volume and high concentration of LA is associated with a higher success rate and shorter onset time than high volume and low concentration solution. Therefore, we think that low volumes and high concentrations of LA may have an effect on axillary block and postoperative analgesia. However, to our knowledge, there is no study reporting LA dose, LA concentration and LA type in NIRS administration.

Conclusion

After the axillary block, it was determined that measuring StO2 using NIRS is a useful method to evaluate the success of the block. It was concluded that axillary block application is a successful and reliable method for patients undergoing upper extremity surgery. It was recommended to include axillary block in routine practice and use it more frequently in upper extremity surgeries. It was also concluded that further studies are needed in this regard.

Acknowledgements: *none*

Ethical Approval: *The study protocol was approved by the Harran University, Faculty of Medicine, Clinical Research Ethics Committee (Date 12/12/2014 Meeting Number: 26).*

Author Contributions: *Concept: MS, MAK, ŞY Literature Review: MAK,MS,AY Design: MS,NA,EB Data acquisition: MS,ŞY,EB Analysis and interpretation: MS,MAK,NA Writing manuscript: MAK,MS,AY Critical revision of manuscript: ŞY,MAK*

Conflict of Interest: *The author(s) do not have any potential conflict of interest regarding the research, authorship and/or publication of this article.*

Financial Disclosure: *This thesis was supported by Harran University Scientific Research Board with the date 22.04.2015 and project number 15068.*

References

1. Moorthy SS, Schmidt SI, Dierdorf SF, et al. A supraclavicular lateral paravascular approach for brachial plexus regional anesthesia. Anesth Analg1991;72 (2): 241- 4.
2. Brown DL, Bridenbaugh LD. The upper extremity-somatic block. In: Neural blockade in clinical anesthesia and management of pain. M.J. Cousine, P.O. Bridenbaugh (Eds) 3rd edition Lippincot Raven. 1998; 345-72.
3. Ting PL, SivagnanaratnamV. Ultrasonographic study of the spread of local anaesthetic during axillary brachial plexus block. Br J Anaesth 1989 63(3): 326-9
4. Sebastiani A, Philippi L, Boehme S, et al. Perfusion index and plethysmographic variability index in patients with interscalen nevre catheters. Can J Anaesth. 2012; 59 (12): 1095-101.
5. Cannesson M, Desebbe O, Rosamel P,et al.Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic wave form amplitude and predict fluid responsiveness in the operating theatre. Br J Anaesth 2008;101(2) :200–6.
6. Cohn SM. Near-infrared spectroscopy: potential clinical benefits in surgery. J Am Coll Surg. 2007;205(2):322-32.
7. Barker SJ, Shande A, Ramsay MA. Continuous Noninvasive Hemoglobin Monitoring: A Measured ResponseTo A Critical Review, Anesth Analg. 2016; 122(2): 565-72.
8. Minville V, Gendre A, Hirsch J,et al. The Efficacy of Skin Temperature for Block Assessment After Infraclavicular Brachial Plexus Block, Anesth Analg. 2009;108(3):1034-6.
9. Collins VJ. Regional Anesthesia. In: Collins VJ. (Ed.). Principles of Anesthesiology: General and regional anesthesia. 3rd ed. Philadephia: Lea&FebigerCo; 1993: 1445-571.
10. Liu GY, Chen ZQ, Jia HY, et al. The technique comparison of brachial plexus blocks by ultrasound guided with blocks by nevre stimulator guided. Int J ClinExpMed. 2015 15;8(9):16699-703.
11. Elshamaa HA. Stress response in shoulder surgery under interscalene block, randomized controlled study comparing ultrasound guidanceto nevre stimulation. Saudi J Anaesth. 2015; 9(4):359-64.
12. Çelik E, Kavak GÖ. Evaluation of Brachial Plexus Block With PlethysmographicVariability Index and Perfusion Index. Journal of Harran University Medical Faculty. 2021;18(2):170-5.
13. Okano T, Okuda Y, Kimura Y, et al. Use of near-infrared spectroscopy to evaluate stellate ganglion block. Reg Anesth Pain Med 2001; 26(2): 186-7.
14. Tsai PB, Tokhner V, Li J, et al. A new application fornear-infrared spectroscopy in regional anesthesia? JAnesth. 2011; 25(1):140-1.
15. Tighe PJ, Elliott CE, Lucas SD ,et al. Noninvasive tissue oxygen saturation determined by near-infrared spectroscopy following peripheral nevre block. Acta Anaesthesiol Scand. 2011; 55(10):1239-46.
16. Karahan MA, Binici O, Büyükfırat E. Tissue Oxygen Saturation Change on Upper Extremities After Ultrasound-Guided Infraclavicular Brachial Plexus Blockade; Prospective Observational Study. Medicina (Kaunas). 2019 14;55(6):274.
17. Topçam T, Özden MGN, Kocaarslan C, et al. Effect of Brachial Plexus Block on Tissue Oxygenation in Arteriovenous Fistula Surgery: A Randomized Clinical Trial. GKDA 2022;28(3):247-53.

IJCMBS

THE INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND BIOLOGICAL SCIENCES e-ISSN: 2791-8815

Orgınal Article

Analysis of disturbution of bronchopulmonary segments in covid-19 patients

Covid-19 hastalarında bronkopulmoner segmental dağılımın analizi

Ayşe Gül Kabakci[1*], Yeşim Taşova[2], Memduha Gülhal Bozkir[3]

[1]*Department of Anatomy, Faculty of Medicine, Cukurova University, Adana, Turkiye*
[2] *Infectious Diseases and Clinical Microbiolog, Faculty of Medicine, Cukurova University, Adana, Turkiye*
[3]*Department of Anatomy, Faculty of Medicine, Cukurova University, Adana, Turkiye*

**Corresponding author:*
Dr. Ayşe Gül Kabakcı,Ph.D.

Adress: Ayşe Gül Kabakci, Cukurova University Faculty of Medicine Deparment of Anatomy, Balcalı, Sarıçam, Adana,Turkiye.

E-mail: akabakci@cu.edu.tr
Received: 07/08/2023
Accepted: 06/11/2023
Cite as: KABAKCI. A.G. and et al. Analysis of disturbution of bronchopulmonary segments in covid-19 patients . IJCMBS 2023;3(3):162-8 doi.org/10.5281/zenodo.10141163

Highlights

• We found that the lower lobe of the right lung was the most affected from the COVID-19.

• The lower lobe posterior segment was mostly affected in men, while the lower lobe superior and lateral segments were affected in women.

Abstract

Background: Imaging modalities are important in the correct treatment and diagnosis of COVID 19, which causes severe damage to lung tissue. Ground-glass opacity is the most commonly reported imaging finding of COVID-19 pneumonia. Therefore, we aimed to analyze the distribution of bronchopulmonary segments in patients with ground-glass opacities.

Materials and Methods: We included tomography images of 93 patients who were diagnosed as COVID-19 positive during the period when COVID-19 vaccine studies had not yet started. Thorax CT images of patients with COVID-19 were examined in the axial line. In each slice, the presence of ground-glass image of the right and left lungs was examined segment by segment. All slices with ground-glass image were recorded for each patient according to the slices in the Radiopeadia program.

Results: The mean age of patients with ground-glass opacity was 47.05±16.35 years (21-82), 45.77±16.15 years in men and 48.58±16.76 years in women. In addition, the mean age of 36 patients (19 males and 17 females) without ground glass opacity was 44.28±17.53 years. When the right and left lungs were compared by gender, the density of ground-glass opacity was 50.17% in men and 49.83% in women in the right lung, and 56.40% in men and 43.6% in women in the left lung. When the right and left lungs were compared, the presence of ground-glass opacities was observed in 56.18% of the right lung and 43.82% of the left lung. **Conclusion:** In our study, we found that most ground glass opacity appearance were observed in the lower lobe, right lung and in men. We think that this study will be a source of data on the course of the COVID 19 in the medium and long term.

Key Words: Bronchopulmonary segments, COVID-19, Glass opacity, Lung

ÖZ

Amaç: Akciğer dokusunda ciddi hasara neden olduğu görülen COVID 19'un doğru tedavi ve tanısında görüntüleme yöntemleri önemlidir. Buzlu cam opasitesi, COVID-19 pnömonisinin en sık bildirilen görüntüleme bulgusudur. Bu nedenle çalışmamızda buzlu cam opasiteleri olan hastalarda bronkopulmoner segmentlerin dağılımını analiz etmeyi amaçladık.

Gereç ve Yöntem: COVID-19 aşı çalışmalarının henüz başlamadığı dönemde COVID-19 pozitif tanısı alan 93 kişinin tomografi görüntülerini çalışmaya dahil ettik. COVID-19'lu hastaların toraks BT görüntüleri aksiyel hatta incelendi. Her kesitte sağ ve sol akciğerlerin buzlu cam görüntüsünün varlığı segment segment incelendi. Radyopeadya programındaki kesitlere göre her hasta için buzlu cam görüntüsü olan tüm kesitler kaydedildi.

Bulgular: Buzlu cam opasitesi saptananların yaş ortalaması 47.05±16.35 (21-82) yıl olup, erkeklerde 45.77±16.15, kadınlarda 48.58±16.76 idi. Ayrıca, buzlu cam opasitesi bulunmayan 36 kişinin (19 erkek ve 17 kadın) yaş ortalaması 44.28±17.53'tür. Sağ ve sol akciğerler cinsiyete göre karşılaştırıldığında, sağ akciğerde erkeklerde %50,17 ve kadınlarda %49,83, sol akciğerde ise erkeklerde %56,40 ve kadınlarda %43,6 oranında buzlu cam opasitesi yoğunluğu kaydedilmiştir. Sağ ve sol akciğerler karşılaştırıldığında, buzlu cam opasitelerinin varlığı sağ akciğerde %56,18 oranında, sol akciğerde ise %43,82 oranında gözlenmiştir.

Sonuç: Çalışmamızda en fazla buzlu cam görünümünün alt lobda, sağ akciğerde ve erkeklerde tutulum gösterdiğini bulduk. Bu çalışmanın orta ve uzun vadede COVID 19'un seyri hakkında veri kaynağı oluşturacağını düşünüyoruz.

Anahtar Kelimeler: Bronkopulmoner segmentler, COVID-19, Buzlu cam görüntüsü, Akciğer

Introduction

There have been approximately 8 million confirmed cases and more than 425,000 confirmed deaths due to COVID-19, a large family of viruses that can cause serious illness (1). In many countries, CT is the important method for identifying and triaging COVID-19 patients. The first study on chest CT findings of COVID-19 was published in January 2020. In the study, it was revealed that most of the hospitalized patients with bilateral lung involvement had ground glass opacities (GGO) (2).

Intense acute respiratory syndrome has been reported in studies to cause serious damage to lung tissue. Therefore, CT imaging is important in accelerating the evaluation for correct treatment. Moreover, in the literature, studies have been conducted on clinical, epidemiological features and potential risk factors in patients with COVID-19 with a poor prognosis by clinicians (3-5)

Ground glass opacity is the most common finding of COVID-19 pneumonia with a rate of 40-83% on imaging (6). For this reason, we included patients who were followed up and treated in our hospital, diagnosed with COVID-19 with lung CT examination. The evaluations were made according to gender. In the bronchopulmonary segmental distribution examinations in our study, we aimed to reveal intensive the pulmonary prognostication during the period when COVID-19 vaccine studies had not yet started. We think that this study will guide both the current pandemic situation and future pandemics by creating basic data. Because, thanks to past pandemics, preparations can be made against possible pandemics again. In addition, there are data on long-term pulmonary sequelae after COVID-19 in studies investigating the radiologic findings of COVID-19 in the lung in the literature (7). In this study, our aim was to establish a basis with CT findings for the comparison of short- and long-term segmental lung involvement after COVID-19 before and after vaccine administration.

Material and Method

This study was conducted retrospectively. The informed consent was waived due to the retrospective nature of the study and the assessment utilized anonymous research findings. CT images were interpreted by the same infectious specialist and lung segmental distribution was made by the same anatomists. The relevant guidelines and regulations were strictly followed when conducting the study. Ethic committee approval for the study were obtained from Cukurova University Medical Faculty, Non-invasive clinical research Ethic Board (132/30). In addition, necessary permissions were obtained from the Department of Infectious Diseases and Clinical Microbiology. The experimental procedures were conducted in accordance with the Declaration of Helsinki.

Study Design

First of all, a list of patients who were diagnosed with COVID-19 in March, 2020-July, 2020 from the Department of Infection And Clinical Microbiology was obtained. This list included 93 people who were COVID-19 positive and had a CT image. Secondly, the presence of GGO in the CT images of the COVID-19 positive people on this list in the Department of Infectious Diseases and Clinical Microbiology was checked. It was determined that 57 of 93 people with glass opacities in the CT images. Assessment of anatomical lung segment was performed on CT images (Toshiba Aquilion™ PRIME; Otawara, Japan).

Computed Tomography Protocol

Firstly, a list of patients who were diagnosed with Covid-19 positive from the Infection and Clinical Microbiology Department. Secondly, CT images were randomly selected from the archive for our retrospective study. All CT images were obtained using a 160-slice MDCT scanner (Toshiba Aquilion™ PRIME; Otawara, Japan). Thoracic CT images of patients with COVID-19 were examined on the axial line.

Bronchopulmonary Segments Analysis

First, the presence of GGO was determined in each segment of the right and left lung lobes of each patient. The segment to which the detected GGO presence corresponded was recorded using Radiopedia (Radiopaedia.org) program. Confirmation of the segment name according to the Radiopedia program ensured the objectivity of the analysis (Figure 1). Radiopaedia is a program that aims to educate radiologists, other healthcare professionals and medical students accurately and free of charge in all areas related to the practice of medical imaging. The naming of the segments in the three lobes of the right lung are as follows; upper lobe: apical, posterior, anterior, middle lobe: lateral, medial and lower lobe: superior, medial, anterior, lateral, posterior. In addition, the naming of the segments in the left lung; upper lobe: apicoposterior, anterior, superior lingular, inferior lingular and lower lobe: superior, anteromedial, lateral, posterior (Figure 1).

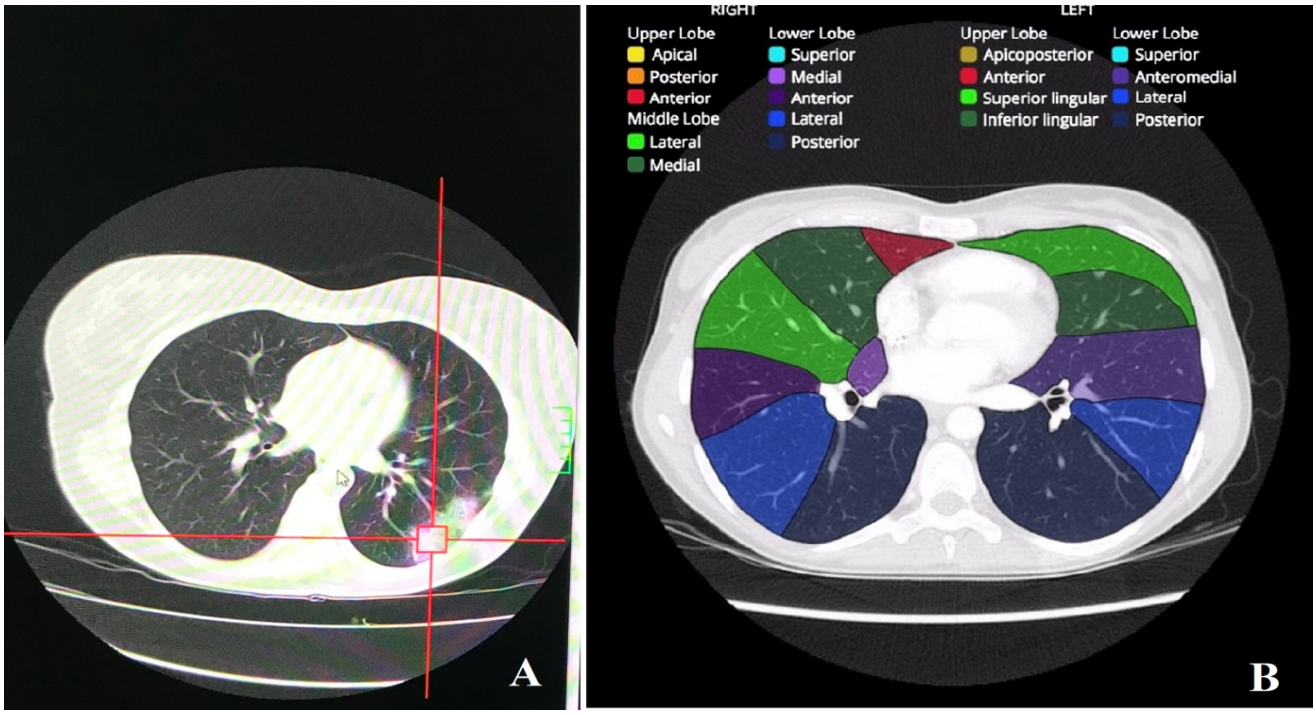


Figure 1. Determination of bronchopulmonary segment analysis via CT image (A) and the radiopeadia program image (B)

Statistical Analysis

Statistical analysis was performed through the SPSS v.22 package program (IBM SPSS Statistics, Chicago, IL, USA). The relationship between the age, gender and GGO was calculated through the "Pearson's correlation coefficient test." The intraclass correlation coefficient (ICC) test was used to analyze intraobserver reliability for repeated measurements with a 95% confidence interval. ICC was interpreted as follows: Below 0.50: Poor; between 0.50 and 0.75: Moderate; between 0.75 and 0.90: Good; and above 0.90: Excellent. A p=0.05 was considered statistically significant. Also, categorical variables were assessed as frequency and percent rates (%) with graphics.

Results

In our study, we found that 57 of 93 COVID-19 patients had ground glass opacities (GGO). Of these 57 patients, 31 were male and 26 were female. The mean age of those with GGO was 47.05±16.35 (21-82) years, 45.77±16.15 for men and 48.58±16.76 for women. In addition, the mean age of 36 subjects without GGO (19 males and 17 females) was 44.28±17.53 years. We analyzed the correlation of age and gender with GGO and found a weak negative correlation between age and GGO (r=-0.081, p=0.440). We also found a weak positive correlation between gender and GGO (r=0.016, p=0.881). When the right and left lungs were compared, the presence of GGO was observed in 56.18% of the right lung and 43.82% of the left lung (Figure 2).

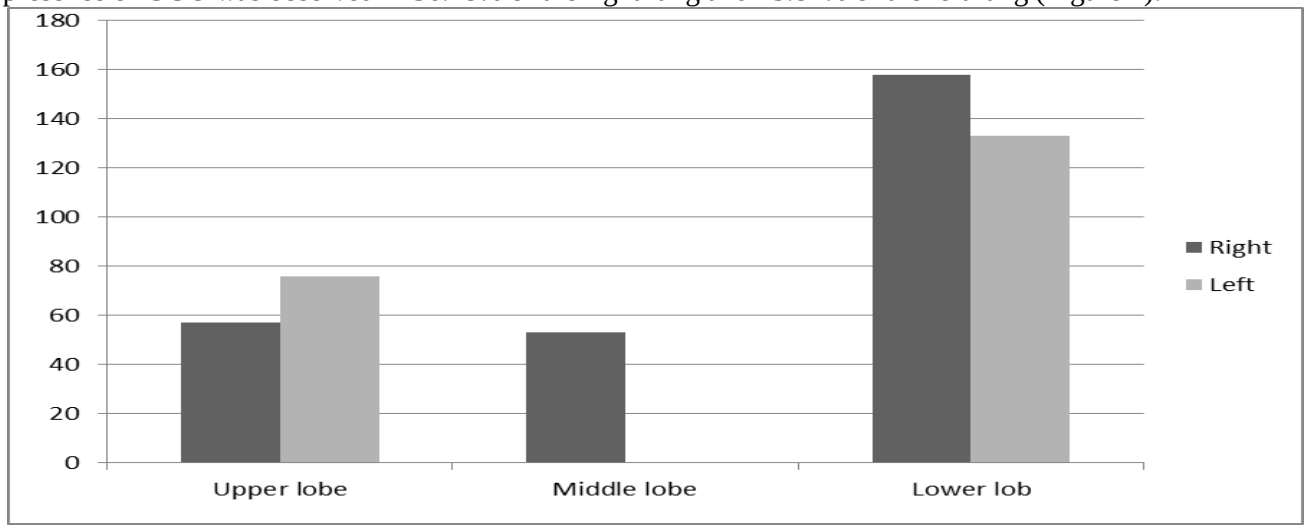


Figure 2. Distribution of ground glass opacities according to lobes in right and left lungs

The segmental distribution of GGO in the right lung was 21.27% in the upper lobe, 19.78% in the middle lobe and 58.95% in the lower lobe (Figure 3A). In addition, GGO density was observed in the posterior segment of the upper lobe (9.33%), lateral segment of the middle lobe (10.07%) and lateral (13.81%) and posterior (13.81%) segments of the lower lobe in the right lung (Figure 3A). In the left lung, the segmental distribution of GGO was 36.36% in the upper lobe and 63.64% in the lower lobe (Figure 3B). Furthermore, GGO density was observed in the superior lingular segment with a rate of 10.53% in the left lung upper lobe and in the posterior segment with a rate of 19.14% in the left lung lower lobe (Figure 3B).

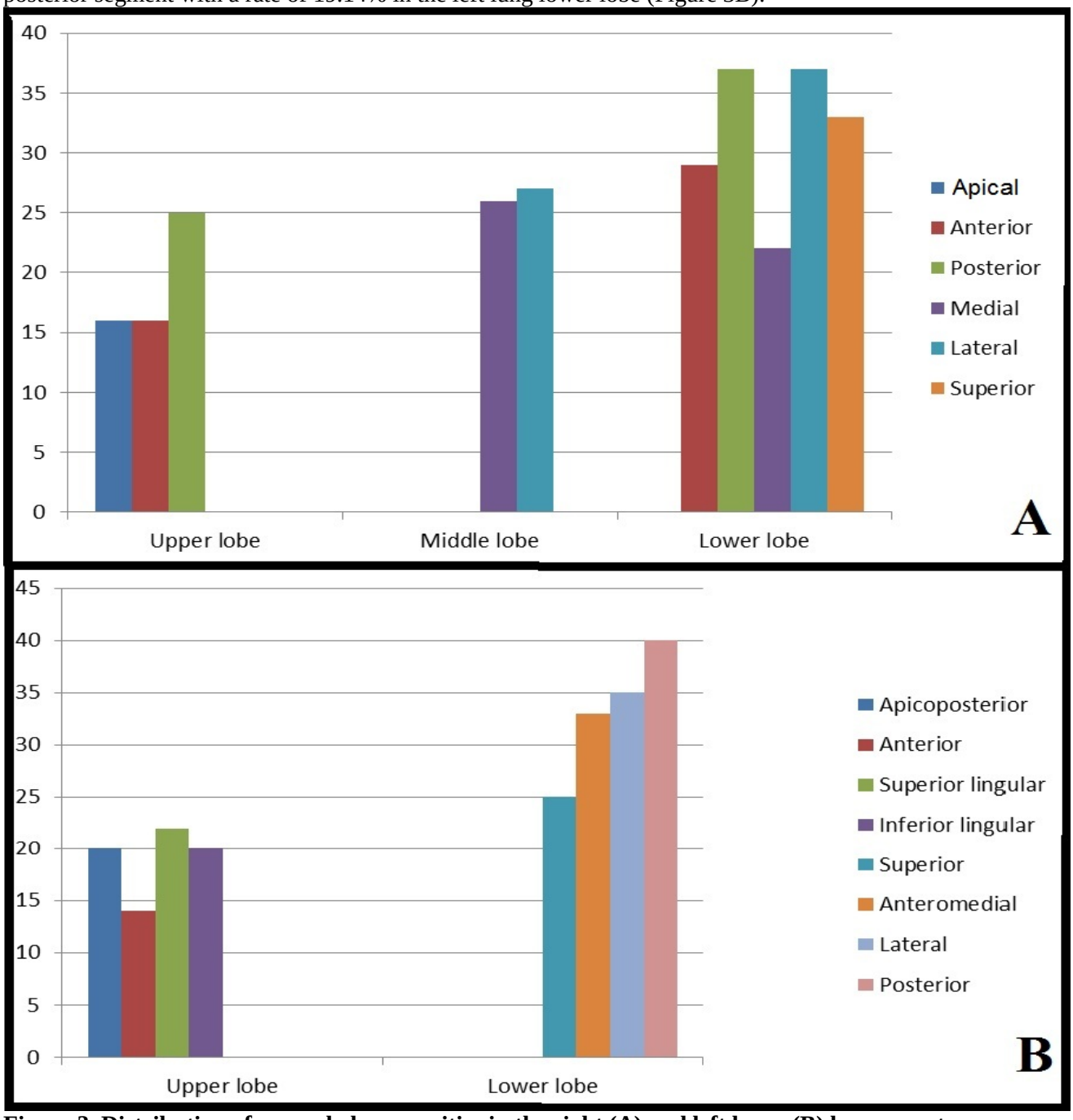


Figure 3. Distribution of ground glass opacities in the right (A) and left lungs (B) by segments

When the right and left lungs were compared by gender, GGO density was 50.17% in males and 49.83% in females in the right lung and 56.40% in males and 43.6% in females in the left lung (Figure 4).

In addition, the presence of GGO in the right lung was 11.94% in the upper lobe, 10.82% in the middle lobe and 33.96% in the lower lobe in men, compared to 9.33% in the upper lobe, 8.95% in the middle lobe and 25% in the lower lobe in women (Figure 5C). Furthermore, the presence of GGO in the left lung was 20.40% in the upper lobe and 33.83% in the lower lobe in men, compared to 17.41% in the upper lobe and 28.36% in the lower lobe in women (Figure 5A). On the other hand, the segmental density distribution of GGO in the right lung was 9.87% in the upper lobe posterior segment, 10.53% in the middle lobe lateral segment and 15.79% in

the lower lobe posterior segment in men (Figure 5D), compared to 8.62% in the upper lobe posterior segment, 11.21% in the middle lobe medial segment and 14.66% in the lower lobe posterior segment in women (Figure 5D). Similarly, the segmental density distribution of GGO in the left lung was 6.47% in the upper lobe apicoposterior segment and 11.44% in the lower lobe posterior segment in men (Figure 5B) and 5.97% in the upper lobe superior lingular segment and 8.46% in the lower lobe posterior segment in women (Figure 5B).

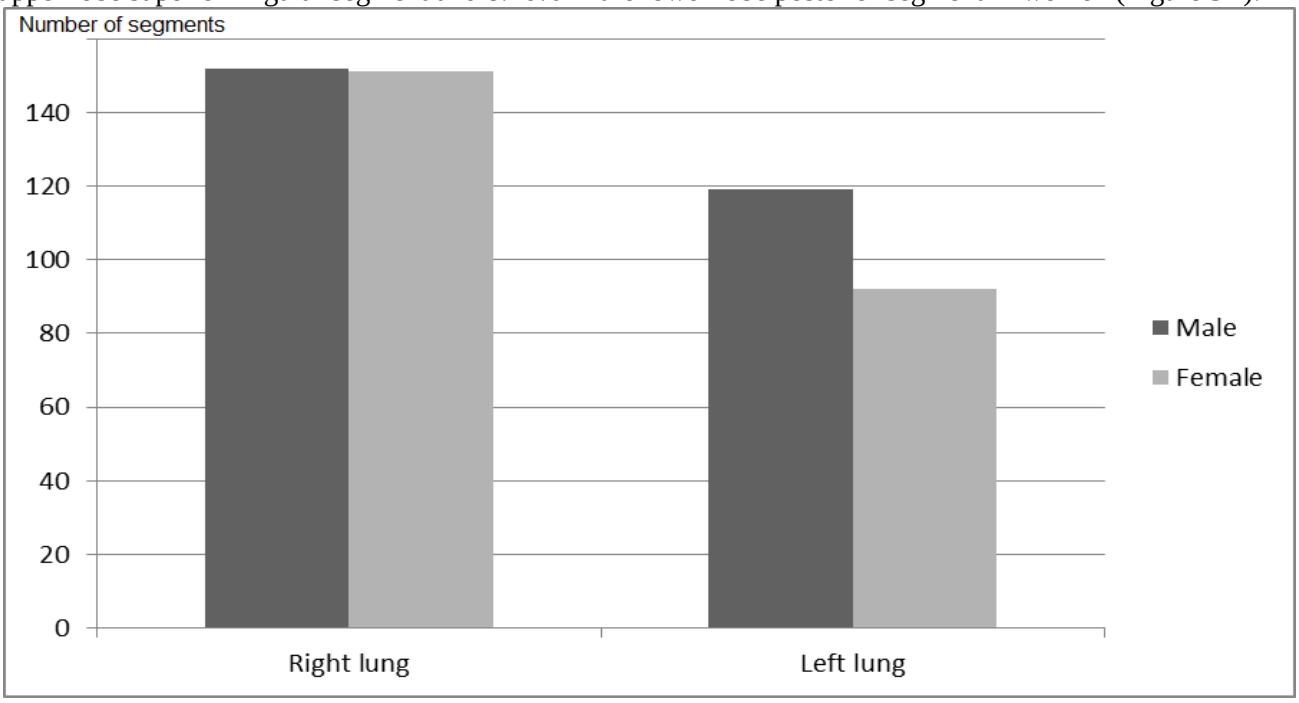


Figure 4. Distribution of ground glass opacities in the right and left lungs by gender

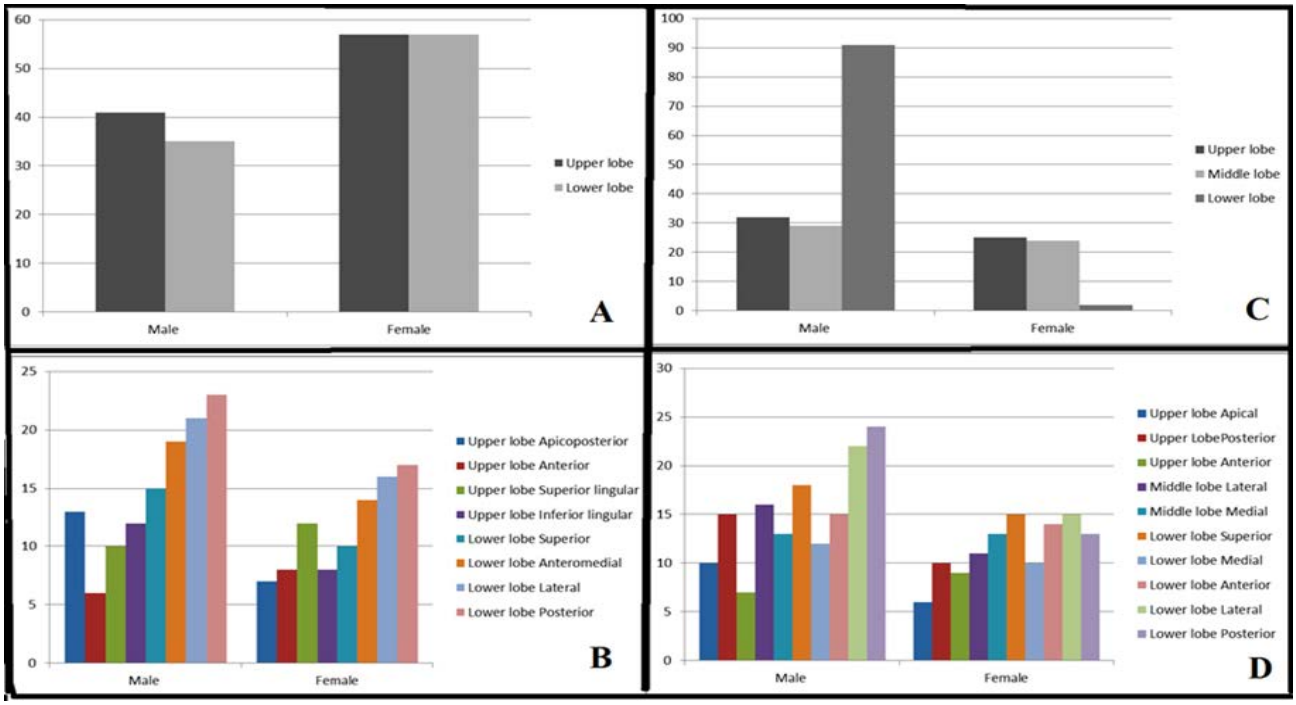


Figure 5. Distribution of ground glass opacities according to segments in the right (C and D) and left (A and B) lungs by gender

Discussion

The most common finding in the lungs during COVID-19 diagnosis is ground-glass opacities (GGO) (8). Therefore, we examined the pulmonary segmental distribution of GGO in our study. In this way, the presence of GGO in the right and left lungs was mostly seen in the lower lobe. In addition, more GGO was detected in the right lung than in the left lung. In the right lung, most glass opacities were observed in the lower lobe

posterior and lateral segments. In addition, the right lung upper lobe posterior segment and the middle lobe lateral segment had the most GGO appearance. On the other hand, the highest GGO in the left lung upper lobe was observed in the superior lingular segment. Similar to our study, it has been reported in the literature that the characteristic findings of COVID19 pneumonia are predominantly localized in the lower lobes (9). In addition, Salehi et al. (10) revealed that the posterior regions of the lungs were affected by COVID-19 with a rate of 80%. Similarly, Özmen's study showed that COVID-19 pneumonia is characterized by bilateral, peripheral, round GGO predominantly located in the posterior lower lobes (11). In another study, Litmanovich et al. (12) reported that GGO was commonly located in the lower lobe of the lung in their Chest Radiography Findings. These results were also consistent with our study. The predominant distribution of GGO in the lower lung can also be interpreted as findings specific to COVID-19 pneumonia, but may overlap with other infections, drug reactions, and other causes of acute lung injury. Conversely, the atypical appearance of the GGO image may indicate that COVID-19 may also affect other lung segments. Moreover, in our study, the condition of 36 COVID-19 patients without GGO may show that there is no sign of pneumonia. However, chest CT findings may also show that COVID-19 pneumonia may have disappeared in the early period.

Furthermore, when we evaluated by gender, GGO was most common in males. In addition, the right lung was most commonly involved in both sexes. In the right lung, men were mostly affected in the upper lobe posterior segment, middle lobe lateral segment and lower lobe posterior segment, whereas women were mostly affected in the upper lobe posterior segment, middle lobe medial segment and lower lobe lateral and superior segments. We also found that the apicoposterior segment of the upper lobe and the posterior segment of the lower lobe of the left lung were most affected in men, whereas the superior lingular segment of the upper lobe and the posterior segment of the lower lobe were most affected in women. However, we found that although the appearance of GGO was more common in men, the upper lobe of the right lung was more affected in women. Karacan et al. and Gu et al. examined the variability of chest CT findings of COVID-19 according to age and gender and found that older and male patients were more affected (13,14). In our study, similar to the literature, GGO was found more frequently in men. In addition, Xudong et al. similarly found that the distribution of lesions in the right lobe was higher in men in an artificial intelligence study conducted in young and middle age group (15). In conclusion, the results of our study before vaccination and the results of the studies in the literature after vaccination were found to be similar.

Study Limitations

The limitations of this study are that it was a single-center study, which limits its generalizability. The study was conducted before vaccines against COVID-19 became available, so the clinical situation and management of patients with severe COVID-19 may have changed, as fewer patients now progress to acute respiratory failure. Therefore, a limitation of our study is the absence of findings from the pre-vaccination period as well as post-vaccination period. Furthermore, the main limitation of this study is the inclusion of a small population. We recommend studies with a larger number of patients, using different methods and influencing factors (chronic disease, smoking, inflammation markers, etc.) to determine the severity of pulmonary involvement in the pre-vaccination period and post-vaccination period.

Conclusion

We found that the lower lobe of the right lung with the densest GGO image and the most affected right lung was found in COVID-19 patients. In addition, the lower lobe posterior segment was mostly affected in men, while the lower lobe superior and lateral segments were affected in women. Although many discoveries have been made regarding the pathogenesis and treatment of COVID-19, we believe that this study will be a source of data on the course of the disease in the medium and long term. We also believe that our study analyses will contribute to the rapid triage and evaluation of acute patients suspected of having COVID-19, as studies in the literature have done.

Acknowledgements: *none*

Ethical Approval: *The study protocol was approved by the Cukurova University, Faculty of Medicine, Non-invasive clinical research Ethic Board (Date 07/04/2023, Meeting Number: 132/30).*

Author Contributions: *Concept: AGK, YT, MGB Literature Review: AGK, YT, MGB Design: AGK, YT, MGB Data acquisition: AGK, YT Analysis and interpretation: AGK, YT, MGB Writing manuscript: AGK, YT, MGB Critical revision of manuscript: AGK, YT, MGB.*

Conflict of Interest: *The authors do not have any potential conflict of interest regarding the research, authorship and/or publication of this article.*

Financial Disclosure: *none*

References

1. Yuan Y, Jiao B, Qu L, et al. The development of COVID-19 treatment. Front Immunol. 2023;14:1125246.
2. Cao B, Iredell J, Middleton P, et al. Chest CT in COVID-19 patients: A clinical need. J Med Radiat Sci. 2023;70(1):40-45.
3. Xu B, Martín D, Khishe M, Boostani R. COVID-19 diagnosis using chest CT scans and deep convolutional neural networks evolved by IP-based sine-cosine algorithm. Med Biol Eng Comput. 2022;60(10):2931-2949.
4. Çelik B, Karaca B. New regular candidates to the emergency department; lasting symptoms following acute COVID -19 infection: the example of northwestern Syria. International Journal of Current Medical and Biological Sciences. 2022;2(2):96-102.
5. Yasak İH, Yılmaz M, Seyhanlı ES, Gönel A. Relationship between Coronavirus Disease and Erythrocyte Morphology Parameters. International Journal of Current Medical and Biological Sciences. 2022;2(3):192-198.
6. Ye Z, Zhang Y, Wang Y, et al. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol. 2020;30(8):4381-9.
7. Brieghel C, Ellekvist P, Lund ML, et al. Prognostic factors of 90-day mortality in patients hospitalised with COVID-19. Dan Med J. 2021;68(3):A09200705.
8. Kovács A, Palásti P, Veréb D, et al. The sensitivity and specificity of chest CT in the diagnosis of COVID-19. Eur Radiol. 2021;31(5):2819-24.
9. Raptis CA, Hammer MM, Short RG et al. Chest CT and coronavirus disease (COVID-19): a critical review of the literature to date. Am J Roentgenol. 2020;215(4):839-42.
10. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. Am J Roentgenol. 2020;215(1):87-93.
11. Özmen CA. The radiology of COVID-19 pneumonia. Dicle Med J. 2021;48(Special Issue):5-14.
12. Litmanovich DE, Chung M, Kirkbride RR, et al. Review of chest radiograph findings of COVID-19 pneumonia and suggested reporting language. J Thorac Imaging. 2020;35(6):354-360.
13. Karacan A, Kurt Z, Taydaş O, et al. A comparison of computerized tomography findings of COVID-19 infection by gender and age groups. Rev Assoc Med Bras. 2021;67(4):542-548.
14. Gu Q, Ouyang X, Xie A, et al. A retrospective study of the initial chest CT imaging findings in 50 COVID-19 patients stratified by gender and age. J Xray Sci Technol. 2020;28(5):875-884.
15. Xudong Y, Weihong L, Feng X, et al. Artificial intelligence-based CT metrics used in predicting clinical outcome of COVID-19 in young and middle-aged adults. Med Phys. 2022;49(8):5604-5615.