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#### List of the reviewers who reviewed papers for Eurasian Journal of Emergency Medicine December 2023.

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Eurasian Journal of Emergency Medicine (Eurasian J Emerg Med) is the open access, scientific publication organ of the Emergency Physicians Association of Turkey that is published in accordance with independent, unbiased, double blind peer review principles. The journal is published 4 times in a year in March, June, September and December.

The journal aims to publish scientifically high quality articles which can contribute to the literature and written in the emergency medicine field and other related fields. Review articles, case reports, editorial comments, letters to the editor, scientific letters, education articles, original images and articles on history and publication ethics which can contribute to readers and medical education are also published.

The journal's target audience includes Emergency Medicine experts, School members who conduct scientific studies and work in the Emergency Medicine field, researchers, experts, assistants, practicing physicians and other health sector professionals.

Editorial and publication processes of the journal are shaped in accordance with the guidelines of the international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE). The journal is in conformity with Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

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Editorial and publication processes of the journal are shaped in accordance with the guidelines of the international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE). The journal is in conformity with Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/ bestpractice).

Originality, high scientific quality and citation potential are the most important criteria for a manuscript to be accepted for publication. Manuscripts submitted for evaluation should not be previously presented or published in an electronic or a printed medium. Editorial Board should be informed of manuscripts that have been submitted to another journal for evaluation and rejected for publication. Submission of previous reviewer reports will expedite the evaluation process. Manuscripts that have been presented in a meeting should be submitted with detailed information on the organization including the name, date and location of the organization.

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2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND

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**Review Articles:** Reviews which are prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into high volume of publication and higher citation potential are taken under review. The authors may be invited by the journal. Reviews should be describing, discussing and evaluating the current level of knowledge or topic used in the clinical practice and should guide future studies. Please check Table 1 for limitations for Review Articles.

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**Clinical Imaging / Visual Diagnosis:** Images must be typical for diagnosis, and should facilitate rapid diagnosis for emergency medicine and / or should be educational. Except for the header and references, it must consist of maximum 400 words. A maximum of three authors name, six images and five refecences should be included.

**History:** This type of manuscript explains events related to emergency and general medicine and presents information on the history of diagnosis and treatment of diseases. Historical findings should be a result of relevant research studies. Manuscript should not include sub-headings, should not exceed 900 words and total number of references should be limited to 10. **Publication ethics:** This type of manuscript includes current information on research and publication ethics and presents cases of ethics infringement. Main text should not exceed 900 words and total number or references should be limited to 10.

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Tables should be included in the main document, presented after the reference list and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide an easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

Table 1. Limitations for each manuscript type.					
Type of manuscript	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	5000 (Structured)	200	50	6	7 or total of 15 images
Review Article	5000	200	50	6	10 or total of 20 images
Case Report	1500	200	10	No tables	10 or total of 20 images
Letter to the Editor	500	N/A	5	No tables	No media
Scientific letter	900	N/A	10	No tables	2 or total of 4 images
Clinical Imaging/ Visual Diagnosis	400	N/A	5	No tables	3 or total of 6 images
History	900	N/A	10	No tables	3 or total of 6 images
Publication ethics	900	N/A	10	No tables	No media

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Figures, graphics and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labelled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks and similar marks can be used on the images to support figure legends. Like the rest of



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All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and the main text. The abbreviation should be provided in parenthesis following the definition.

When a drug, product, hardware, or software mentioned within the main text product information, including the name of the product, producer of the product, city of the company and the country of the company should be provided in parenthesis in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

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Limitations, drawbacks and shortcomings of original articles should be mentioned in the "Discussion" section before the conclusion paragraph.

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While citing publications, preference should be given to the latest, most up to date publications. If an ahead of print publication is being cited the DOI number should be provided. Authors are responsible for the accuracy of references. Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/ Medline/PubMed (for journal abbreviations consult the List of Journals indexed for MEDLINE, published annually by NLM). When there are 6 or fewer authors, all authors should be listed. If there are 7 or more authors the first 6 authors should be listed followed by "et al". In the main text of the manuscript, references should be cited using Arabic numbers in parentheses. The reference styles for different types of publications are presented in the following examples:

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**Book Section:** Sherry S. Detection of thrombi. In: Strauss HE, Pitt B, James AE, editors. Cardiovascular Medicine. St Louis: Mosby; 1974.p.273-85.

**Books with Single Author:** Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Marcel Dekker; 1993.

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the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992.p.1561-5.

**Scientific or Technical Report:** Smith P. Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX) Dept. of Health and Human Services (US). Office of Evaluation and Inspections: 1994 Oct. Report No: HHSIGOE 169200860.

**Thesis:** Kaplan SI. Post-hospital home health care: the elderly access and utilization (dissertation). St. Louis (MO): Washington Univ. 1995.

Manuscripts accepted for publication, not published yet: Leshner AI. Molecular mechanisms of cocaine addiction. N Engl J Med In press 1997.

**Epub ahead of print Articles:** Sarıtaş A, Güneş H, Kandiş H, Çıkman M, Çandar M, Korkut S, et al. A Retrospective Analysis of Patients Admitted to our Clinic with Aortic Dissection. Eurasian J Emerg Med 2011 Dec 10. doi:10.5152/jaem.2011.035. [Epub ahead of print]

**Manuscripts published in electronic format:** Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL:http://www.cdc.gov/ncidodIEID/cid.htm.

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The reviewers review the manuscript.

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The decision letter is sent to the author.

The reviewers are expected to focus on the following issues:

#### 1. General recommendation about the manuscript

How original is the manuscript?

Is it well presented?

What is the length of the manuscript?

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How important is the manuscript in this field?

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Are statistical analyses appropriate?

#### Are the results presented clearly?

Does the discussion cover all of the findings?

Are the references appropriate for the manuscript?

#### 4. Remarks to the editor

Accepted in its present form

Accepted after modest revisions

Reconsidered for acceptance after major changes

Rejected

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What would be your recommendations to the author?

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# Attack on Health Care Workers: A New Complex Cancerous Humanitarian Emergency: High Time to Report and Resect

## Tanmoy Ghatak, D Utsav Anand Mani

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Keywords: Emergencies, conflict, attack on healthcare, Global Health Security, WHO Surveillance System

Healthcare workers (HCWs) are becoming common soft target these days. Attacks on them are a serious and growing problem all over the world, increasing with intolerance among the public. According to the World Health Organization (WHO), there will be over 1,500 reported attacks on HCWs in 2022 alone, resulting in at least 180 deaths and countless injuries (1). Attacks can take many forms, including physical violence, verbal abuse, and threats or intimidation. The consequences of attacks on HCWs can be devastating. They can lead to physical injury, psychological trauma, and even death. Attacks can also damage health care facilities and disrupt the delivery of essential services, hampering the achievement of universal health coverage-an initiative for the right to health (2). Sensing the range of adversities of attacks on health care, the WHO developed the Surveillance System of Attacks on Healthcare and Health Care at Risk (SSA) in December 2017 to monitor the issue (3). WHO field officers along with their partners gather data in those areas on the ground and contribute incidents directly into the SSA database.

In this issue of the journal, the article titled "Attacks on Health Care Worldwide: 5-year Review" addresses the grave issue of attacks on healthcare services (4). This retrospective study explores and explains the data of the five-year period from January 1, 2018, to November 11, 2022, from the SSA databases. The authors' aim is to bring attention to this critical problem while calling for new international initiatives to combat it. These alarming data underscore the perilous conditions faced by health services and workers, particularly in conflict zones and during global health crises such as the Coronavirus disease-2019 (COVID-19) pandemic and Ebola outbreaks. The key findings reveal a staggering number of attacks, not only particularly in conflict war zones such as the occupied Palestinian Territory and Ukraine but also in other countries such as Afghanistan, the Syrian Arab Republic, and Yemen, resulting in numerous injuries and deaths among HCWs and damage to healthcare facilities. Despite existing international regulations such as the Geneva Convention, these attacks persist (5). The figures also reflect that heavy weapons as well as individual weapons are frequently in use. This affects not only combatants but also civilian access to healthcare services. Such attacks are not limited to war zones but also occur in peacetime, exacerbated by pandemics such as COVID-19. We agree that these attacks can lead to secondary health crises, such as migration and the spread of epidemics due to disruptions in healthcare services (6).

Violence against HCWs is actually less reported. Actually, the reported cases we are seeing are just the tip of the iceberg. Mediatrial, negative media marketing like highlighting any HCWs small fault, and less strict laws in protection cause lesser reporting of cases. When we see the SSA inclusion countries, we can see that only 24 countries are involved in data generation. Therefore, it might not have captured worldwide data, echoing the fact. Data from large population countries such as China, America, and India are missing.

Our editorial focuses on the humanitarian crisis precipitated by persistent attacks on healthcare services, emphasizing the need for immediate and concerted global action to protect HCWs and maintain the sanctity of medical facilities as neutral zones in conflict areas. We also underscore the broader implications of



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these attacks on global health security and the urgent need for more robust reporting and accountability mechanisms. A united international response and strict sanctions against such acts of violence are the need of the hour. We as emergency physicians feel that the emergency department and emergency medicine services are more prone to violence compared to other areas of the hospital and healthcare as we are in fore front. A systematic review of the literature has emphasized that violence against emergency medical personnel is not an isolated occurrence but a widespread issue affecting these critical frontline workers globally (7). In 2017, the academic college of emergency experts academy of family physicians of India alerted all about the issue through their position paper stating the Indian scenario and the way outs (8). The call to action for the international community to respond collectively and enforce serious sanctions is critical. It emphasizes the need for a unified approach to prevent such attacks and to hold accountable those who perpetrate them. Without concerted international efforts, including punitive resective measures, this cancerous situation is unlikely to improve. It is an ethical imperative for the global community to protect healthcare services, which are vital to the well-being and dignity of individuals, especially during conflicts and crises.

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Eurasian J Emerg Med. 2023;22(4): 211-5

# Attacks on Health Care Worldwide: 5-year Review

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## Abstract

Aim: The aim of our study is to explore the attacks on healthcare services and bring attention to this problem and raise awareness of the need for new national and international initiatives in this area.

**Materials and Methods:** The databases Surveillance System for Attacks on Health Care and Attacked and Threatened: Health Care at Risk were scanned between January 1, 2018 and November 11, 2020 to gather the research data (5 years).

**Results:** When the attacks are evaluated by country or region, it has been revealed that the Occupied Palestinian territory reported the most incidences with 1,140 (28.64%) attacks, followed by Ukraine with 666 (16.73%) attacks on healthcare facilities. As a result of the attacks, the Occupied Palestinian Territory experienced the most injuries with 695 people (53.1%), Afghanistan had the most deaths with 63 people (18.9%), and the most healthcare facility damage occurred with 581 (33.8%) organizations in Ukraine.

**Conclusion:** Despite the worldwide standards and national regulations of the Geneva Convention; attacks on healthcare personnel continue unabated, particularly in war and conflict zones. Reports from numerous nations and locations worldwide confirm this.

Keywords: Disaster medicine, emergencies, conflict, attack on healthcare

# Introduction

The World Health Organization defines violence as "the intentional use of physical force or power, threatened or actual, against oneself, another person, or a group or community that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment, or deprivation" (1,2). Violence can be collective like war or systematic like terrorism, whereas other forms of violence include acts of violence against women and even acts of self-harm. Nevertheless, social violence is also influenced by acts of violence committed by individuals (3).

Violence is one of the most significant issues of our time. It is difficult to consider attacks on health services, buildings, vehicles, and equipment as violent acts. This circumstance can only be understood as a state of madness or part of a conflicting war strategy in places of chaos and disarray. At some point in their employment, 8% to 38% of healthcare professionals worldwide are subjected to physical violence. The prevalence of verbal and psychological abuse and threats to significantly higher than that of physical violence. Research reveals that regardless of a country's level of development, violence against healthcare staff is a pervasive problem. In recent years, it has been reported that global health-related violence has increased. However, it is difficult to determine the true prevalence of incidents due to difficulties in accessing data, a lack of systematic studies, and a lack of reporting (4-6).

The persistence of attacks on healthcare services, even when healthcare personnel perform under extremely difficult conditions and jeopardize their own health, just like during the Coronavirus disease-2019 (COVID-19) pandemic, demonstrates the need for extensive public work and the implementation of appropriate measures. The global scope of the problem is revealed by the World Medical Association's report on the rise in violence in healthcare and its declaration as an international emergency (7).

We wanted to draw attention to this issue by analyzing the attacks on healthcare services in the last 5 years. We wanted to raise awareness that attacks on healthcare services are not declining despite the existence of several international regulations and



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© Copyright 2023 The Emergency Physicians Association of Turkey / Eurasian Journal of Emergency Medicine published by Galenos Publishing House Licenced by Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) 4.0 International License. restrictions and that additional efforts should be made on a global basis.

## **Materials and Methods**

The research is a cross-sectional retrospective study. The databases Surveillance System for Attacks on Health Care (8) and Attacked and Threatened: Health Care at Risk (9) were scanned between January 1, 2018 and November 11, 2020 to gather the research data (5 years). Ethics committee approval was not obtained as data from open-access sources and a database that can be accessed publicly were used.

## **Statistical Analysis**

Frequency data are presented as numbers and percentages in descriptive analyzes while continuous numerical data are given using the arithmetic mean and standard deviation. The chi-square ( $\chi^2$ ) test was used to compare categorical data.

The statistical significance level for all tests was set as p<0.05.

## Results

Over the course of five years, 3,980 attacks on healthcare services were reported. 1,095 people were killed and 2,697 were injured in these attacks. These reports were made from 18 countries or territories. One thousand seven hundred twenty-one healthcare facilities were damaged, 2,153 healthcare personnel were injured, and 485 patients were harmed in these attacks. In the

attacks, 100 people were injured at most in a single occurrence and 87 people were killed at most.

Considering the number of attacks by year, the highest number of attacks was reported in 2019 with 1,032 (25.9%). Eight hundred-two (20.2%) attacks on healthcare services were reported in 2018, 344 (8.6%) in 2020, 834 (21%) in 2021, and 968 (24.3%) in 2022 (Table 1).

Reviewing the Attacked and Threatened: Health Care at Risk system reveals that 6,109 reports have been made globally for all reasons related to healthcare services. Examining the number of incident-specific notifications reveals that 6,872 (86.40%) assaults for which the cause can be established were due to conflict, 149 (1.87%) due to COVID-19, 168 (2.11%) due to Ebola, 727 (9.14%) due to political causes, and 38 (%) due to vaccination (Table 2).

Evaluating the attacks by country or region (Table 3), it was determined that the Occupied Palestinian Territory had the highest number of occurrences with 1,140 (28.64%) attacks, followed by Ukraine with 666 (16.73%) attacks. The Occupied Palestinian Territory has the highest number of attack-related injuries with 695 people (53.1%) and the highest number of attack-related deaths with 63 people (18.9). Most healthcare facility damage has occurred in Ukraine, with 581 (33.8%) organizations sustaining damage.

The reported attacks affected 180 (4.5%) tertiary healthcare institutions, 529 (13.3%) secondary healthcare institutions, and

Table 1. Number of attacks and results by year							
Years	Attacks	Injuries	Fatal Injuries	Affected patients	Affected health facilities	Affected health personnel	
2018	802 (20.15%)	899 (33.33%)	158 (14.43%)	77 (15.88%)	212 (12.32%)	533 (24.76%)	
2019	1032 (25.93%)	634 (23.51%)	201 (18.36%)	68 (14.02%)	329 (19.12%)	687 (31.91%)	
2020	344 (8.64%)	322 (11.94%)	243 (22.19%)	52 (10.72%)	179 (10.40%)	175 (8.13%)	
2021	834 (20.95%)	424 (15.72%)	279 (25.48%)	176 (36.29%)	338 (19.64%)	465 (21.60%)	
2022	968 (24.32%)	418 (15.50%)	214 (19.54%)	112 (23.09%)	663 (38.52%)	293 (13.61%)	
Total	3980 (100%)	2697 (100%)	1095 (100%)	485 (100%)	1721 (100%)	2153 (100%)	
Source: Surveillan	Source: Surveillance System for Attacks on Health Care						

Table 2. Number of attacks on health services by incident category							
	Conflict	COVID-19	Ebola	Political	Vaccination		
Health facilities damaged	3676 (53.49%)	42 (28.19%)	53 (31.55%)	20 (2.75%)	1 (2.63%)		
Health workers kidnapped	630 (9.17%)	14 (9.40%)	21 (12.50%)	5 (0.69%)	14 (36.84%)		
Health workers injured	1795 (26.12%)	81 (54.36%)	67 (39.88%)	681 (93.67%)	11 (28.95%)		
Health workers killed	771 (11.22%)	12 (8.05%)	27 (16.07%)	21 (2.89%)	12 (31.5%8)		
Total	6872 (100%)	149 (100%)	168 (100%)	727 (100%)	38 (100%)		
Source: Attacked and Threatened: Health Care	Source: Attacked and Threatened: Health Care at Pick. COVID-19: Coronavirus disease-2019						

803 (20.2%) primary healthcare institutions. The reported attacks caused the most damage to healthcare facilities in Ukraine. In terms of healthcare facility involvement, a statistically significant difference was found between attacks in which heavy weapons were reported and other attacks (p<0.001, x<sup>2</sup>=551.823).

Individual weapons were used in 1,497 (37.6%) of the attacks; heavy weapons were used in 1,289 (32.4%); sexual assault was committed in 11 (0.3%); and 852 (21.4%) psychological violence has been reported (Table 4).

There were 1,309 injuries and 339 fatalities among the reported incidents (Table 5). It was determined that 63% of the injuries occurred in attacks where individual weapons were used, 23.3% in attacks in which heavy weapons were used, and 14.9% in attacks in which individual and heavy weapons were involved together. In terms of injuries, there was a significant difference between the attacks in which individual weapons were used and those in which heavy weapons were used (p<0.01,  $x^2=141,652$ ).



# Discussion

This study demonstrates that despite the worldwide standards and national regulations of the Geneva Convention, violence related to the provision of healthcare services persists and attacks against healthcare professionals have not decreased (10,11). Many patients injured people, and civilians have had difficulty accessing health care as a result of violence and attacks on healthcare facilities. It is extremely difficult to determine the extent to which these attacks affect healthcare workers, particularly in conflict zones. For this, well-structured and effective notification systems are needed. As a result, it is believed that many healthcare worker deaths are misclassified as civilian deaths (12).

Although we want to draw attention to violence and attacks on healthcare in our study, it is seen that the incidents intensify in war and conflict zones. The damage caused by attacks on healthcare services or healthcare workers is not limited to the attack itself but has a knock-on effect that can deprive patients of treatment and lead to a wave of migration (13). The murder of six ICRC health workers in December 17, 1996 and the suspension of the organization's operations in Chechnya are two such examples. According to the study, this single event deprived thousands of war-wounded patients of surgical care (14).

Table 4. Types of attacks on health care				
Types of attack	n	%		
Individual weapons	1497	24.33		
Heavy weapons	1289	20.95		
Psychological violence	852	13.85		
Obstruction	679	11.04		
Removal assets	435	7.07		
Removal personal	384	6.24		
Assault	379	6.16		
Violent search	325	5.28		
Militarization	146	2.37		
Setting fire	123	2.00		
Chemical agents	17	0.28		
Criminalization of health care	12	0.20		
Sexual assault	11	0.18		
Unknown	8	0.13		
Source: Surveillance System for Attacks on Health Care				

When the situations involving attacks and violence are examined, it is seen that there are different numbers of notifications in the same time period in different tracking and registration systems in the regions. It is thought that the recording of tracking systems with a common method and the sharing of data can eliminate this problem (8,9).

The magnitude of the additional costs that arise as a result of attacks on healthcare facilities and personnel may not be accurately determined at the first stage. Secondary losses are significantly greater than primary losses. Disruptions in emergency healthcare services and primary healthcare services as a result of healthcare access issues may result in even higher costs than the picture revealed by the war (15,16). Furthermore, this situation is closely related to civilian protection (12).

In our study, we discovered that attacks involving only individual weapons resulted in more deaths and injuries than attacks involving heavy weapons. The destructive potential of weapons also rises alongside technological progress. Although heavy weapons have a greater destructive power, individual weapons also have a high destructive power (17,18). The higher number of casualties in attacks involving individual weapons is often attributed to the increased likelihood of target shooting. For this reason, keeping in mind that more deaths and injuries occur in individual or light weapon attacks on health services, appropriate measures should be taken in areas of conflict and war.

## **Study Limitations**

Since our study is an open-access database study, it was not possible to obtain all of the requested data. An evaluation was made using the data presented.

# Conclusion

Over the past five years, it has been observed that attacks on healthcare services have not diminished. On the other hand, attacks are concentrated in areas where confusion and conflict exist. It is one of the most important findings of our study that the highest number of attacks and related injuries and deaths occurred in the Palestinian territories, the highest number of healthcare facility damages occurred during the Ukrainian War, and individual weapons were most commonly used to inflict injuries during attacks on health services. The fact that attacks on healthcare services in these regions have not decreased despite

Table 5. Comparison of the types of weapons used in attacks and their effects									
Weapon type     Injuries     Fatal injuries     Affected health care worker					are worker				
Individual weapons	722 (63.2%)	p<0.001	170 (58.2%)	p<0.05	923 (69.5%)	p<0.001			
Heavy weapons	421 (36.8%)	x <sup>2</sup> =141,652	122 (41.8%)	x <sup>2</sup> =8,815	406 (30.5%)	x <sup>2</sup> =387,263			
Source: Surveillance System for	Attacks on Health Car	ρ		Source: Surveillance System for Attacks on Health Care					

numerous international regulations suggests that this situation has been adopted as a strategy. Disrupting combatants' access to healthcare services and demoralizing them may be one of these objectives. However, another consequence is that it is difficult for civilians to access healthcare services, and they are forced to leave their areas of residence. Disruptions in vaccination studies, noncompliance with the rules governing women's and reproductive health, hygiene, sanitation, and disruption of fundamental public health services in these regions cause secondary problems such as the spread of epidemics. Even though the number of attacks for other motives is relatively low, they should not be underestimated. For this reason, the international community should act collectively against attacks on healthcare services, and serious sanctions should be applied.

#### Ethics

**Ethics Committee Approval:** Ethics committee approval was not obtained as data from open-access sources and a database that can be accessed publicly were used.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

#### **Authorship Contributions**

Surgical and Medical Practices: F.C.T., Concept: F.C.T., Design: F.C.T., F.S.Ö., Data Collection or Processing: F.C.T., Analysis or Interpretation: F.C.T., F.S.Ö., Literature Search: F.C.T., Writing: F.C.T., F.S.Ö.

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# Comparison of MGAP, GAP, and RTS for Predicting Early Mortality in Multiple Trauma Patients

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## Abstract

Aim: Trauma scoring systems help physicians recognize trauma severity. The purpose of this study was to compare the diagnostic accuracy of the revised trauma score (RTS), Glasgow coma scale (GCS), age, and arterial pressure (GAP), and the mechanism of GCS, age, and arterial pressure (MGAP) to predict early in-hospital mortality.

Materials and Methods: This was a retrospective cross-sectional study of multiple trauma patients who presented to the emergency department from March 2021 to December 2021. The GAP, MGAP, and RTS scores were calculated according to the physiological variables collected by the pre-hospital emergency system personnel. The area under the receiver operating characteristic (AUROC) curve was used to compare all scores in predicting 24-h mortality.

Results: Of the 263 patients included in this study, 19 (7.2%) died within 24 h. The mean age was 38.23±15.75 years, and 82 (31.2%) patients were female. The survived and non-survived patients had significant differences in age (p=0.004), systolic blood pressure (p<0.001), heart rate (p=0.001), and GCS (p<0.001). AUROCs of RTS, GAP, and MGAP scores to predict 24-h mortality were 0.921 [95% confidence interval (CI): 0.882-0.951], 0.909 (95% CI: 0.867-0.941), and 0.898 (95% CI: 0.855-0.932), respectively. There was no significant difference in the scores for predicting the early mortality rate.

Conclusion: The RTS, GAP, and MGAP scores were good predictors of 24-h mortality, and they were similar in predicting early mortality in multiple trauma patients.

Keywords: Emergency, mortality, injury, scoring system

# Introduction

Trauma is one of the most important public health challenges worldwide. Following the advancement of science and technology and the industrialization of societies in the last century, trauma and its complications are now the most common causes of death and disability in people aged 1-44 (1,2).

Trauma is among the four leading causes of death in developing countries such as Iran and the second leading cause of death

among young people (1,3). Iran has one of the highest mortality rates from road accidents. Every year, 27,000 deaths and approximately 240,000 injuries occur due to road accidents (4).

Trauma is a time-sensitive condition. Correct and effective management of trauma patients in pre-hospital and hospital settings helps reduce mortality and prevent complications (4). The main goals of managing trauma patients include quick assessment of critically ill patients, determining treatment



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priorities, and providing appropriate care services. Scoring systems are a tool used to achieve these goals. They are very useful tools for estimating patient outcomes such as mortality and trauma complications. The first scoring system for trauma patients was introduced approximately 60 years ago, but to date, many changes have been made (5).

There are two different types of trauma scoring systems. The first type is measured on the basis of the severity and anatomical location of the injuries. The Injury Severity Score is an anatomy-based score and was introduced in 1974 by Baker et al. (6). The second type of scoring system is based on the physiological response of the injured patient. One of the physiological scoring systems used to evaluate trauma patients is the revised trauma score (RTS). RTS was first designed and evaluated on the basis of a study with more than 2000 patients (7). The RTS consists of three physiological parameters: Glasgow coma scale (GCS), systolic blood pressure (SBP), and respiration rate (RR) (7,8).

In addition, two modified scoring systems, MGAP (mechanism of injury, GCS, age, and arterial pressure) and GAP (GCS, age, and arterial pressure) score, have been designed to predict survival in trauma subjects (3). GAP consists of Age, GCS, and SBP. The mechanism of injury is also included in the MGAP (9). Variables in GAP and MGAP are easily available at the time of admission. Regarding MGAP, there is a debate on how to score the mechanism of trauma. In this system, penetrating trauma is given a higher score, whereas penetrating trauma is not always more severe than blunt trauma (9,10). The scoring systems are effective not only in the appropriate triage of patients but also in predicting the severity of injury and mortality of patients (10-12).

The purpose of the present study was to evaluate and compare the diagnostic accuracy of RTS, GAP, and MGAP in predicting early in-hospital mortality of patients with multiple trauma referred to the emergency department (ED) in a regional trauma center in Rasht, Iran.

# **Materials and Methods**

## **Study Setting and Design**

This was a retrospective cross-sectional study that was conducted on patients with multiple trauma presenting to the ED of Poursina Hospital, Rasht, Iran, from March 2021 to December 2021. The study protocol was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1400.519, date: 26.01.2022).

## **Participants**

Adult multiple trauma patients with triage levels 1, 2, and 3 were eligible to participate in the study. The triage level was determined on the basis of the Emergency Severity Index (ESI) version 4 in the ED triage unit. ESI is a five-level ED triage modality that clinically classifies patients into five groups from 1 (most urgent) to 5 (least urgent) based on severity and resource requirements (1). Patients younger than 18 years who died before ED of, transferred from other medical centers, pregnant women, and those who had missing variables were excluded.

### **Data Gathering**

Data were collected by reviewing patient case histories. The data included patient demographic characteristics (gender, age) and the mechanism of trauma at admission. The RTS, GAP, and MGAP scores were calculated according to the physiological variables (SBP, RR, and GCS) collected by the pre-hospital emergency system personnel.

#### Measurements

The RTS consists of three physiological parameters (GCS, SBP, RR). RTS=0.9368 GCS + 0.7326 SBP + 0.2908 RR. The total score is between 0 and 7.8408 (7). A lower RTS score indicates higher severity of the injury.

GAP consists of three parameters: physiological and age. The patient received 3 to 15 scores based on GCS score and three scores for age <60 years. They also received six scores for SBP >120 mmHg and four for SBP of 60-120 mmHg (13). The total score was between 3 and 24, with a lower score predicting a worse prognosis.

MGAP was calculated by adding the mechanism of trauma (blunt or penetrating) to the GAP score. The patient received 3 to 15 scores based on GCS score, five scores for ages 60 years, and four scores for blunt injury. They also received five scores for SBP >120 mmHg and three for SBP of 60-120 mmHg (9). Total scores ranged from 3 to 29, with higher scores being indicative of a better prognosis.

The primary outcome was early mortality. Early mortality was defined as patients who died due to multiple traumas within 24 h after admission to the hospital. The accuracy of the RTS, GAP, and MGAP scores with this outcome was investigated.

### **Statistical Analysis**

The minimum sample size was 245 subjects based on the results of a previous study (14) on the GAP score, assuming a sensitivity of 64%, a confidence level of 95%, and a type-2 error of 6%, according to the following formula: Sampling was performed using the consecutive sampling method.

$$n = \frac{z_{1-\alpha/2}^2 \times sen (1-sen)}{d^2}$$

Variables were analyzed using Statistical Package for the Social Sciences (IBM, Armonk, NY, version 21.0). Patient data were reported as frequency (%), mean±standard deviation (SD), or 95% confidence interval (CI). Fisher's exact test, independent samples t-test, or Mann-Whitney U test were used to compare variables.

The area under the receiver operating characteristics curve (AUROC) was used to determine the discriminating power of the RTS, GAP, and MGAP to predict 1-day mortality. Sensitivity, specificity, positive and negative likelihood ratios, and positive and negative predictive values (PPV and NPV) were plotted for each score. P value <0.05 was considered significant.

## Results

Two hundred and sixty-three multiple trauma patients were included. The mean (SD) age was 38.23 (15.75) years, and 82 (31.2%) patients were female. The 24-h mortality rate was 19 patients (7.2%). Motor vehicle accidents were the leading cause of injury (60.5%). Baseline characteristics are reported in Table 1.

The median (interquartile range) RTS, GAP, and MGAP scores were 7.1 (6.17-7.84), 21 (18-22), and 24 (22-27), respectively. The RTS, GAP, and MGAP scores were significantly higher in the survived patients than in the non-survived patients (p<0.001). The survived and non-survived patients had significant differences in age (p=0.004), SBP (p<0.001), heart rate (p=0.001), and GCS (p<0.001).

The AUROCs of RTS, GAP, and MGAP scores to predict 24-h mortality were 0.921 (95% CI: 0.882-0.951), 0.909 (95% CI: 0.867-0.941), and 0.898 (95% CI: 0.855-0.932), respectively (Figure 1). The optimal cut-off points for the RTS, GAP, and MGAP scores were  $\leq$ 5.98,  $\leq$ 18, and  $\leq$ 21. The RTS, GAP, and MGAP scores were good predictors of 24-h mortality. RTS was similar to GAP (p=0.533) and MGAP (p=0.289) in predicting 24-h mortality. The NPVs of RTS, GAP, and MGAP for 24-h mortality were 99.0%, 99.0%, and 98.5%, respectively (Table 2).

## Discussion

The primary goal of trauma patients is their survival. Therefore, identifying patients at risk of death is important. For this purpose, triage and scoring systems have been used to identify critically ill patients. These systems are effective not only in determining

Table 1. Comparison of demographic and clinical characteristics of multiple trauma patients according to in-hospital mortality						
Characteristics		Total (n=263)	Survived (n=244)	Non-survived (n=19)	p value	
Age, mean±SD, year		38.23±15.75	38.02±16.28	50.78±19.78	0.0041	
Conder n (0/)	Female	82 (31.2)	79 (32.4)	3 (15.8)	0.1002	
	Male	181 (68.8)	165 (67.6)	16 (84.2)	0.196	
Mechanism, n (%)	Motor vehicle accidents	159 (60.5)	150 (61.5)	9 (47.4)		
	Pedestrian accidents	40 (15.2)	36 (14.8)	4 (21.1)		
	Fall	28 (10.7)	26 (10.7)	2 (10.5)	0.528 <sup>2</sup>	
	Assault	30 (11.4)	26 (10.7)	4 (21.1)		
	Others	6 (0.2)	6 (2.5)	0 (0.0)		
	3-8	13 (4.9)	7 (2.9)	6 (31.6)	< 0.001 <sup>2</sup>	
Classow come scale n (0/)	9-12	11 (4.2)	7 (2.9)	4 (21.1)		
Glasgow coma scale, n (%)	13-14	10 (3.8)	9 (3.7)	1 (5.3)		
	15	229 (87.1)	221 (90.6)	8 (42.1)		
	HR; bpm	87.48±13.98	86.98±13.68	96.78±21.13	0.001 <sup>1</sup>	
Initial vital signs, mean±SD	SBP; mmHg	130.05±19.36	131.01±17.12	121.09±16.75	< 0.0011	
	RR; bpm	19.27±3.55	19.33±3.12	20.02±6.48	0.072 <sup>1</sup>	
	RTS	7.1 (6.17-7.84)	7.2 (6.81-7.84)	5.14 (4.2-5.14)	< 0.0013	
Scores, median (IQR)	GAP	21 (18-22)	21 (19-22)	13 (8-16)	< 0.0013	
	MGAP	24 (22-27)	24 (22-27)	18 (12-21)	< 0.0013	

IQR: Interquartile range, SD: Standard deviation, HR: Heart rate, SBP: Systolic blood pressure, RR: Respiratory rate, RTS: Revised trauma score, GAP: Glasgow coma scale, Age, and arterial pressure, MGAP: Mechanism, Glasgow coma scale, age, and arterial pressure, CI: Confidence interval <sup>1</sup>Analyzed using independent-samples t-test.

<sup>2</sup>Analyzed using Fisher's exact test.

<sup>3</sup>Analyzed using the Mann-Whitney U test.

the prognosis of trauma but also in predicting the severity of the injury (6,14,15). The first scoring system for trauma patients was presented approximately 60 years ago, but there have been many changes in this field until today (5).

These scoring systems have limitations and benefits. A good scoring system should have fewer parameters, be easier to use, and be more accurate, especially in emergencies (15). In most multiple trauma patients, the severity of the injury and risk of death can be determined on the basis of physiological parameters in the scene (13). GAP was defined by Kondo et al. (13) in Japan.



Figure 1. Receiver operating characteristic curves of GAP, MGAP, and RTS for predicting early mortality in multiple trauma patients

RTS: Revised trauma score, GAP: Glasgow coma scale, age, and arterial pressure, MGAP: Mechanism, Glasgow coma scale, age, and arterial pressure, ROC: Receiver operating characteristic

The GAP score is easy to use and calculate to determine trauma severity in the early stages (11). The MGAP score was developed by Sartorius et al. (16) as an improvement over the previous trauma scoring systems in France. Another scoring system is RTS, which has limited popularity due to the difficulty of calculation (13,16).

In addition, all scoring systems evaluated in this study (GAP, MGAP, and RTS) are heavily weighted on the GCS to compensate for significant head trauma without multisystem trauma or major physiologic changes. In this study, the predictive value of the three scoring systems in predicting early mortality within 24 h after admission was evaluated. The RTS, GAP, and MGAP scores were good predictors of 24-h mortality, and there was no significant difference between the three scores in predicting early mortality in multiple trauma patients.

In previous studies, a comparison of the scoring systems mentioned above has been made, but in most of them, onemonth mortality or in-hospital mortality was considered. Similar to this study, Ahun et al. (11) compared RTS, GAP, and MGAP for short-term (24 hours) mortality prediction. They found that these scores were significantly associated with short-term mortality. AUROCs were 0.727 for RTS, 0.970 for MGAP, and 0.910 for GAP. The AUROC of MGAP to predict mortality was significantly higher than that of RTS, but there was no significant difference between MGAP and GAP (p=0.177). A multi-center study conducted in Kenya on 16,548 patients demonstrated statistically significantly higher performance of MGAP and GAP than RTS for in-hospital mortality (17).

Farzan et al. (6) reported that MGAP, GAP, and RTS accurately predicted one-month mortality in multiple trauma patients. RTS had slightly better AUROC than GAP and MGAP, but there was no significant difference between them. Mohammed et al. (18) reported that RTS, MGAP, and GAP had good discriminatory ability in predicting the mortality of adult multiple trauma

Table 2. The ROC analysis results of physiologic scoring systems in the prediction of in-hospital mortality						
Variables	RTS	GAP	MGAP			
Cut-off	≤5.98	≤18	≤21			
Sensitivity (95% CI)	89.47 (66.9-98.7)	89.47 (66.9-98.7)	84.21 (60.4-96.6)			
Specificity (95% CI)	84.43 (79.3-88.7)	79.51 (73.9-84.4)	80.74 (75.2-85.5)			
Positive predictive value (95% CI)	30.9 (24.3-38.4)	25.4 (20.3-31.1)	25.4 (19.8-32.0)			
Negative predictive value (95% CI)	99.0 (96.5-99.7)	99.0 (96.3-99.7)	98.5 (95.9-99.5)			
Positive Likelihood ratio (95% CI)	5.47 (4.13-7.99)	4.37 (3.26-5.84)	4.37 (3.17-6.03)			
Negative Likelihood ratio (95% CI)	0.12 (0.134-0.46)	0.13 (0.036-0.49)	0.20 (0.69-0.55)			
AUROC (95% CI)	0.921 (0.882-0.960)	0.909 (0.867-0.941)	0.898 (0.855-0.932)			
p value	<0.001	<0.001	<0.001			
RTS: Revised trauma score, GAP: Glasgow coma scale, age, and arterial pressure, MGAP: Mechanism, Glasgow coma scale, age, and arterial pressure, ALIROC: Area under the						

RTS: Revised trauma score, GAP: Glasgow coma scale, age, and arterial pressure, MGAP: Mechanism, Glasgow coma scale, age, and arterial pressure, AUROC: Area under the receiver operating characteristic, CI: Confidence interval

patients. The AUROC was 0.879, 0.890, and 0.881 for MGAP, GAP, and RTS, respectively, whereas there were no statistical differences between the three scoring systems. These findings were consistent with those of the present study.

In this study, the survived and non-survived patients had significant differences in age, SBP, and GCS, which are the components of GAP and MGAP. RTS ignores the impaired physical resilience associated with aging, and this could be the possible reason for the superiority of GAP and MGAP over RTS in some previous studies (11,17). MGAP and GAP could be more accurately used for injured patients in moderately resourced trauma centers at the time of hospital arrival rather than at a delayed time (18).

Galvagno et al. (19) compared MGAP and RTS to predict in-hospital mortality in trauma patients. They suggested that the MGAP could be a preferable and more easily calculable pre-hospital scoring system. Jeong et al. (20) reported that the accuracy of GAP for the prediction of in-hospital mortality was similar to that of MGAP and significantly better than that of RTS.

Similar to the present study, Yadollahi et al. (3), Soltani et al. (10), and Rahmani et al. (9) showed that there is no significant difference between GAP and MGAP as predictors of mortality in multiple trauma patients. Indeed, the trauma mechanism did not affect the accuracy of scores or patient outcomes. Kondo et al. (13) found that GAP predicted mortality more accurately than MGAP in ED settings. No trauma mechanism score may be effective without an anatomical score. In addition, penetrating trauma subjects comprise less than 10% of the trauma population (3,13,16).

This study found that MGAP and GAP scores can be used as a powerful scoring system for evaluating patient survival in the ED setting. In addition, because of ease of use, the GAP score is more acceptable than MGAP in the triage of trauma patients.

In this study, GAP, MGAP, and RTS had high NPV and low PPV. This may be due to the low prevalence of 24-h mortality (7.2%). Prevalence directly affects NPV and NPV. A reduction in prevalence decreases PPV and an increase in NPV.

## **Study Limitations**

This study has some limitations. First, the present study was retrospective. Second, it was conducted in a single center. Third, the sample size is small. Because the Poursina Hospital was a referral center for COVID-19 until March 2021 it was possible to collect samples from this date onward.

# Conclusion

Rapid and accurate prediction of patients at risk of in-hospital mortality can improve patient outcomes. The RTS, GAP, and MGAP scores were good predictors of 24-h mortality, and they were similar in predicting early mortality in multiple trauma patients. The GAP score is easier to calculate and has fewer variables; therefore, it may be more beneficial to provide quick results and allow for quick decision making. It is a simple and rapid score that can be used for the timely triage of multiple trauma patients in the ED. An early calculation of the GAP score in the triage unit can help allocate needed resources earlier to patients at a higher risk of death and lead to improved trauma management.

## Ethics

**Ethics Committee Approval:** The study protocol was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1400.519, date: 26.01.2022).

Informed Consent: Retrospective cross-sectional study.

Peer-review: Externally and internally peer-reviewed.

### **Authorship Contributions**

Concept: P.A., S.M.Z.Z., F.H., P.M., E.E., N.N.R., Design: P.A., S.M.Z.Z., F.H., P.M., E.E., N.N.R., Data Collection or Processing: P.A., S.M.Z.Z., F.H., P.M., E.E., N.N.R., Analysis or Interpretation: P.A., N.N.R., F.H., Literature Search: P.A., S.M.Z.Z., F.H., P.M., E.E., N.N.R., Writing: P.A., S.M.Z.Z., F.H., P.M., E.E., N.N.R.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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# Characteristics and Clinical Significance of MINOCA Syndrome in Patients with Pre-diagnosis of Acute Coronary Syndrome in the Emergency Department and Performed Coronary Angiography

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## Abstract

**Aim:** Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a condition characterized by clinical findings of acute myocardial infarction (AMI) and detection of normal/close to normal narrowing coronary arteries in coronary angiography (CAG). The aim of this study was to analyze the prevalence and demographic characteristics of MINOCA in a tertiary hospital.

**Materials and Methods:** This observational retrospective study included patients aged 18 years who presented to the emergency department in 2016, met the criteria for universal AMI, and had a CAG of <=50% stenosis. Patients under the age of 18 years and those likely to have a diagnosis other than AMI were excluded.

**Results:** In total, 4197 patients who underwent CAG with a preliminary diagnosis of AMI were evaluated, and 213 patients were included in the study. Of the MINOCA cases, 84 (60.6%) were female and 129 (39.4%) were male. The mean age was 60+/-2 years. Eight (3.8%) patients diagnosed with ST-elevation AMI. There were no ischemic electrocardiographic changes in 91 (42.7%) patients. Hypertension (HT) was the most common comorbidity (53.5%) (n=114). The relationship between advanced age and both in-hospital and 1-year mortality was statistically significant (p<0.005). Strong risk factors affecting the rate of CAG occlusionwere recurrence of AMI, HT, diabetes, and advanced age (p<0.005). Diastolic blood pressure, oxygen saturation, TIMI score, and family history were also factors associated with CAG occlusion rate (p<0.05).

**Conclusion:** There is a need for advanced scoring systems that can be used to define the diagnosis of MINOCA before CAG in emergency services.

Keywords: MINOCA, acute coronary syndrome, normal coronary angiography, emergency department

# Introduction

Chest pain is one of the most common reasons for admission to emergency services and is a major cause of mortality and morbidity. Acute myocardial infarction (AMI) is one of the most important fatal diagnoses to be excluded. Clinical findings of acute myocardial ischemia accompanied by acute myocardial damage and an increase and/or decrease in cardiac troponin values accompanied by at least one of the following findings:

- Myocardial ischemia symptoms,
- New ischemic electrocardiography (ECG) changes,

- Presence of a pathological Q wave,
- Detection of regional wall motion defects that develop newly or are compatible with ischemic etiology,
- Detection of a coronary thrombus by coronary angiography (CAG) or autopsy (1).

Obstructive coronary artery disease (CAD) is defined as >50% stenosis in the coronary arteries of patients undergoing CAG for AMI. A proportion of patients with AMI undergoing CAG does not have clinically significant occlusion of the coronary arteries, which is defined as <50% stenosis. This clinical entity has been



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© Copyright 2023 The Emergency Physicians Association of Turkey / Eurasian Journal of Emergency Medicine published by Galenos Publishing House Licenced by Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) 4.0 International License. described as myocardial infarction with non-occluded coronary artery (MINOCA) (1,2). MINOCA was first included in the literature in the guidelines of the European Society of Cardiology (ESC) in 2017 (2). It is an important syndrome with a prevalence ranging from 2.6% to 15%, and its etiology should be investigated. It is thought that by clarifying the etiology of MINOCA, we can prevent unnecessary CAGs (3).

Among the factors that cause MINOCA, there is a wide spectrum of diseases such as myocarditis, vasospasm, thromboembolism, microvascular dysfunction, oxygen supply/demand mismatch, Takotsubo syndrome, acute pulmonary embolism, coronary thrombosis, and dissection (2-4). Therefore, the diagnostic process may require multiple diagnostic steps such as echocardiography (ECHO), left ventriculography (LVG), intracoronary imaging, computed tomography (CT), pulmonary CT angiography, and cardiac magnetic resonance (CMR) imaging. Etiology research is selected according to the suspected condition, and its treatment is tailored to the needs of the patient (5).

Turkey's population is approximately 84.3 million, and approximately 300,000 cases of AMI are seen in the population every year (6). Therefore, it is important to identify the demographic and clinical characteristics of patients with MINOCA to help create a new strategic plan and approach for these patients in our population. The aim of this study was to investigate the incidence of MINOCA and the demographic and clinical characteristics of these patients in our region.

## Materials and Methods

### **Study Population and Definition**

Our study was retrospectively planned in the Emergency Department of Antalya Training and Research Hospital, a tertiary university hospital in Turkey, after the approval of the ethics committee of the Antalya Training and Research Hospital, numbered 1/3 and dated 11.01.2018. All patients aged 18 years who were diagnosed according to the third universal definition of AMI and underwent CAG in the emergency department between January 1 and December 31, 2016 were included in the study. Accordingly, AMI is defined as clinical evidence of AMI, such as ischemic symptoms along with cardiac biomarker positivity, new ischemic ECG change, pathological Q wave on ECG, and evidence of new viable myocardial tissue loss by imaging (7).

MINOCA definition, as stated in the ESC guide (7); "3. According to the "Universal definitions of AMI", it was accepted as the presence of AMI criteria and the absence of >50% lesions in major epicardial vessels in CAG and the absence of a more probable diagnosis that could be the cause of the acute presentation. The definition of an unoccluded coronary artery is expressed as less than 50% occlusion in the American Heart Association (AHA) and ESC guidelines. The literature also classifies non-occluded vessels into 3; no stenosis is defined as "normal," "plaque" for <30% stenosis, and "mild" occlusion for  $\geq$ 30% but <50% stenosis.

Study data were provided on the basis of cases meeting these definitions.

### **Data Collection**

Patient data were obtained from the hospital's archive. Patients over the age of 18 who met the universal AMI criteria and had ≤50% stenosis at CAG were included in the study. Patients with CAGs from other health centers and/or blood tests performed or diagnosed with a high probability of non-AMI were excluded from the study. In addition, pregnancy was excluded.

Parameters included in the study:

- 1. Sociodemographic characteristics (age, gender),
- 2. Vital signs (temperature, pulse, respiratory rate, systolic and diastolic blood pressure, oxygen saturation) in the emergency room,
- 3. ECG findings in the emergency room,
- 4. Troponin and creatinine levels in the emergency department,
- 5. Type of chest pain,
- 6. Comorbid diseases,
- 7. History of AMI (first/recurrent),
- 8. History of drug/alcohol use and intoxication,
- 9. TIMI score,
- 10. Diagnosis in the emergency room [ST-elevation AMI (STEMI), non ST-elevation MI (NSTEMI)],
- 11. ECO findings [left ventricular wall motion defect, ejection fraction (EF) value],
- 12. CAG and LVG findings,
- 13. Main diagnosis,
- 14. In-hospital and 12-month mortality rates.

A standardized "Study Form" was created for the study, and the information was transferred to the computer environment after recording in this form.

CAG was performed according to the protocols of the catheter laboratory. Patients with <50% occlusion were divided into 3 main groups as normal (0% occlusion), plaque (<30% stenosis),

and mild ( $\geq$ 30%+<50%). Digital copies of CAGs were relieved by 2 different cardiologists who were not familiar with the clinic and the patients, and the diagnosis of MINOCA was confirmed. The mortality status of the patients was obtained from the hospital information management system for in-hospital deaths, and the 1-year mortality was obtained from the Death Information System.

## **Statistical Analysis**

Statistical analysis of the data was performed with Statistical Package for the Social Sciences for Windows 20 package program. Whether the distribution of continuous and discrete numerical variables was close to normal was investigated using the Kolmogorov-Smirnov test. Descriptive statistics are presented as mean±standard deviation for continuous and discrete numerical variables and as number of cases and (%) for categorical variables.

Categorical variables were analyzed using the chi-square test; analysis of parametric data was performed using the Student's t test; Pearson's correlation test was used to compare numerical variables. For p<0.05, the results were considered statistically significant.

## Results

Files of 4197 patients who underwent CAG during the study period were reviewed. Two hundred-thirteen cases (5.04%) were identified as MINOCA. The mean age of the MINOCA population was  $60\pm 2$  years, and 129 patients (60.6%) were female. Table 1 shows the demographic and clinical characteristics of the patients. Only 8 (3.7%) patients with MINOCA were prediagnosed with STEMI in the emergency room. ECG findings were completely normal in 91 (42.7%) patients, non-specific ST-T changes in 64 (30%) patients,

		n	%	p value	Total
Condor	Female	84	39.4	0.16	212
Gender	Male	129	60.6	0.16	215
Drug/alcohol use or intervisation	No	211	99.1	0.02	212
	Yes	2	0.9	0.02	215
Emorgoney room's diagnoso	STEMI	8	3.8	0.96	212
Emergency room's diagnose	NSTEMI	205	96.2	0.86	215
Unarlinidamia	No	195	91.5	0.71	212
пурепірійенна	Yes	18	8.5	0.71	215
	No	99	46.5	<0.005	212
туретензіон	Yes	114	53.5	< 0.005	215
Diabetes mellitus	No	148	69.5	<0.005	212
	Yes	65	30.5	<0.005	215
Smoking	No	169	79.3	0.75	212
	Yes	44	20.7		215
	No	204	95.8	<0.05	213
Family history	Yes	9	4.2		
Malianana.	No	204	95.7	0.00	213
Manghancy	Yes	9	4.3	0.08	
ACC history	First	136	63.8	<0.005	212
ACSTIISTOLA	Recurrent	77	36.2	<0.005	213
Laft ventricle well metion defect	No	136	63.8	0.24	212
Left ventricle wan motion delect	Yes	77	36.2	0.34	213
Mostality	In hospital	3	1.4	<0.005	15
wortanty	In 1 year	12	5.6	<0.005	15
Turne of all out main	Atypical	94	44.1	0.77	212
Type of criest pain	ТурісаІ	119	55.9	0./7	213

coronary syndrome

arrhythmias in 35 (16.4%) patients (ventricular tachycardia, ventricular fibrillation, supraventricular tachycardia, atrial fibrillation), and conduction defects (left bundle branch block, right bundle branch block, and atrioventricular blocks) were found in 23 (10.8%) patients.

When cardiovascular risk factors were examined, 44 (20.7%) patients were smokers, 114 (53.5%) had hypertension (HT), 65 (30.5%) had diabetes mellitus, and 18 (8.5%) had hyperlipidemia (HPL). The mean TIMI score of patients with NSTEMI at admission was 2.37. Left ventricular EF was >50% in 159 (74.6%) patients. While 77 (36.2%) patients had previous CAG with the diagnosis of AMI, 16 (7.5%) had a previous history of coronary artery bypass grafting.

It was determined that the most common chest pain characteristic was the pressure/compression style (55.9%) and was often described as typical chest pain (Table 1).

In our study, the final diagnosis of 99 (46.5%) patients could be determined or the underlying cause could be partially explained, since the etiology research could not be performed in all aspects in our hospital. The final diagnoses are shown in Table 2.

When the TIMI scores of the cases were examined, it was found that those with a TIMI score of 3 were the most (26.3%), those with a TIMI score of 6 were the least (1.4%), and the mean TIMI score was 2.37.

When we analyzed the ECG results in the emergency department, the most common ECG finding of the cases was normal sinus rhythm (n=91) (42.7%), while the patients with blocks (n=23) (10.8%) were the least common (Table 3). In addition, most MINOCA patients diagnosed with NSTEMI (n=205, 96.2%) (Table 1).

Considering the EF values of the patients, the number of patients EF < 40 is 31 (14.6%), the number of patients between 40 and 50 is 23 (10.8%), and the number of patients EF > 50 is 159 (74.6%).

Considering the mortality in MINOCA cases, while there were 3 (1.4%) patients who died in the hospital, 12 (5.6%) people died from all causes within 1 year.

CAG was found to be completely normal in 87 (40.8%) patients. In patients with normal CAG, 4 cases were diagnosed as (1.9%) ectasia, 8 (3.8%) as slow flow, and 3 (1.4%) as spasms in coronaries. In 66 cases (31%), 30-50% stenosis (mild) was found; in 60 cases (28.2%), only plaque was detected.

Previous AMI history, having HT and diabetes comorbid diseases, and advanced age were strong risk factors affecting the rate of CAG occlusion (p<0.005). Occlusion rate was higher in MINOCA

patients with these risk factors. The factors associated with the rate of obstruction in CAG are shown in Table 1. In addition, diastolic blood pressure, oxygen saturation, TIMI score in patients with NSTEMI, and family history were also factors associated with CAG occlusion rate (p<0.05).

Table 2. Distribution of final diagnosis of MINOCA population				
Diagnosis	Frequency (n)	Percent (%)		
No specific diagnosis	114	53.5		
Heart valv pathologies	22	10.3		
Blocs and arrhythmias	22	10.3		
Heart failure	9	4.2		
Coronary slow flow phenomenon	8	3.7		
Ischemic cardiomyopathy	6	2.8		
Takotsubo cardiomyopathy	5	2.3		
Hypertrophic cardiomyopathy	4	1.8		
Dilated cardiomyopathy	3	1.4		
Endomyocarditis	3	1.4		
Drug incompatibility	2	0.9		
Vasospathic angina	2	0.9		
Pericardial effusion	2	0.9		
Coronary ectasia	2	0.9		
Anemia	1	0.4		
Methemoglobinemia	1	0.4		
Peptic ulcer	1	0.4		
Pneumonia	1	0.4		
Postpartum cardiomyopathy	1	0.4		
Right coronary artery outflow anomaly	1	0.4		
String left main coronary artery	1	0.4		
Suicidal drug intake (intoxication)	1	0.4		
Total	213	100.0		
MINOCA: Myocard infarctus with non-obstructive coronary arteries				

Table 3. Distribution of ECG findings of MINOCA population in emergency room					
ECG findings	Frequency (n)	Percent (%)			
Normal sinus rhythm	91	42.7			
Non-specific ST-T changings	64	30.0			
Arrhythmias	35	16.4			
Blocks	23	10.8			
Total	213	100.0			
ECG: Electrocardiyography, MINOCA: Myocard infarctus with non-obstructive coronary arteries					

# Discussion

MINOCA is a syndrome with limited researchand occurs in a small proportion of AMI cases. These patients are often treated conventionally to ensure a good prognosis. The commonly used method for MINOCA risk stratification is angiographic features. Although information on this issue was not provided in previous guidelines, attention was drawn to MINOCA for the first time in the 2017 ESC guideline for the management of AMI in STEMI patients.

Considering the prevalence of MINOCA in the literature, it varies between 2.6% and 15% (7,8). In the multicenter MINOCA-TR study by Kilic et al. (8) in Turkey, the prevalence of MINOCA was found to be 6.7%. In our study, the prevalence of MINOCA was found to be 5.04% in patients with AMI diagnosed in the emergency department, which is consistent with the literature.

When we look at the demographic characteristics, the data on the gender distribution of the MINOCA risk factors are heterogeneous, but it is more common in the female gender (9,10). In contrast, the ESC status report stated that patients with MINOCA were mostly male (2). In a large review conducted in 2018, 60% of patients with MINOCA were male and 40% were female (10). In the MINOCA-TR study female gender was found to be more dominant. As mentioned above, it can be seen that the gender distribution is heterogeneous. In our study, however, we see that the female gender is in the majority and it is compatible with the data of our country.

When we look at the literature for the affected age group, the mean age ranges between 46 and 55 years (11-15). In a 2015 review, the strongest risk factors for MINOCA were female gender and young age. In a study by Agewall et al. (2) in 2016, it was reported that MINOCA patients were younger than those with MINOCA. The mean age of the patients included in our study was 60.04 years. In this context, it is compatible with the literature.

In a study involving only STEMI patients, 58.1% of MINOCA cases presented with typical symptoms (15). This rate is 87.6% in patients with occluded coronary arteries (15). In a large review conducted in 2015, it was found that chest pain was less common in female patients with MINOCA (16). In a gender-focused review conducted in 2016, the most common symptom was typical chest pain (17). Moreover, female patients described chest pain as often crushing, compressive, and constricting and stated that it was accompanied by decreased functional capacity, back pain, and jaw and neck pain (18). In a review of a comprehensive study conducted in 2018, they reported that cases with MINOCA often present with atypical symptoms compared with cases with occluded coronary arteries (12). When we look at the type of chest pain in our study, it is seen that the most common type of pressure/squeeze (26.3%) is the feeling of distress (24.4%) and shortness of breath (18.8%) in the other types. Considering the differences in the literature, it is concluded that MINOCA cases can present with both typical and atypical symptoms. In our study, the patient admitted to the emergency room mainly had typical chest pain, which is compatible with the literature.

When we examine the traditional risk factors of MINOCA, different trends are observed. In a large systematic review conducted in 2015, although the incidence of HPL in MINOCA cases was low, other risk factors were similar (14). According to this study, the rate of HPL was 32% in patients with occluded coronary arteries, whereas this rate was 21% in MINOCA cases, and the difference was found to be significant (14). In a meta-analysis published in 2016, it was reported that diabetes (RR: 0.57), HT (RR: 0.87) and HPL (RR: 0.75), which are classical risk factors, are less common in MINOCA cases (13). In the review published in 2018, the incidence of traditional risk factors was 8.7% in patients with occluded coronary arteries, whereas this rate was 1.3% in MINOCA cases, and the difference was found to be significant (12). Again, in a review published in 2018, HT and diabetes were reported less frequently in MINOCA cases, whereas smoking was more common (odds ratio: 1.9) (10). Among the comorbid diseases in our study, HT (53.5%) was the most common, followed by CAD (36.2%) and diabetes (30.5%). When our study is evaluated in terms of risk factors, it is not compatible with the literature. The fact that the patients included in our study only applied from the emergency department and excluded elective cases may be the reason for this incompatibility. In addition, local comorbidities may differ between regions. Considering that other studies were conducted in European and American societies, we believe that the distribution of comorbidities in the Turkish population may be different.

When we look at the literature, there seems to be only one study evaluating MINOCA patients using risk scoring systems. In a study conducted by Pepine et al. (16) in 2015, the GRACE score was used, and it was found that patients with MINOCA who had a fatal course in the 30-day period had a higher GRACE score at admission than those with MINOCA who were not fatal (14). We used TIMI risk scoring in this study. In our study, the TIMI score was predominantly 3 (26.3%) and generally 1 (19.2%), 2 (21.6%), and 3 (26.3%). The mean TIMI score was 2.37. We found that our patients had a moderate TIMI risk score, but evaluation could not be performed because there is no similar comparison in the literature.

In an evaluation made according to ECG findings, T-segment elevation was found to be 14.8% and non-specific T wave changes were found to be around 60% (19). In the review of the CRUSADE

study in 2009, ECGs of cases with no coronary artery occlusion were examined, and it was found that 71% of MINOCA cases had no ST changes, 21% had ST depression, and 7% had ST elevation (20). In another review published in 2011, ST elevation was found in 36.3% of the cases, ST depression in 15.4%, pathological Q waves in 13.42%, T wave changes in 27.5%, and left bundle branch block in 2.3% (21). In our study, the most common ECG finding was normal sinus rhythm ECG (42.7%), and non-specific ST-T changes (30%) were observed, and the results are consistent with the literature.

There are literature reports that patients with MINOCA were hospitalized with the prediction of severe NSTEMI (2). In 2017, MINOCA was detected in 7% of STEMI cases and MINOCA results in 17% of NSTEMI cases (18). In another large version published in 2017, 8.9% of NSTEMI cases and 1.6% of STEMI cases were diagnosed with MINOCA (10). In a 2016 meta-analysis, MINOCA was found to be less common (RR: 0.20) in STEMI cases (13). Our aim is also compatible with the literature, and we believe that 96.2% of MINOCA patients were hospitalized with predicted NSTEMI.

According to the evaluation of left ventricular wall movements and EFs by transthoracic ECHO, it is stated in the literature that EF is 50% in MINOCA patients (12,13,17,22). According to our study, to consider the heterogeneity in the literature, the mean EF was calculated as 54.6% (+-12.5) and was generally compatible with the literature.

In the review that also formed the basis of the 2017 ESC guideline (18), myocarditis (33%), subendocardial infarct (26%), Takotsubo cardiomyopathy (CMP) (18%), and pericarditis (7%) were determined as the definitive diagnosis after cardiac MRI in the differential diagnosis of MINOCA patients (2,4). However, no diagnosis could be reached by CMR imaging in 26% of the cases. In the same review, provocative spasm testing was performed in 402 MINOCA cases, and inducible spasm was detected in 28-36% of them. The final diagnoses included in the study of 178 cases in which CAG was performed after the preliminary diagnosis of NSTEMI and diagnosed as MINOCA in 2017 (2) were variant angina (10.1%), myocarditis (8.9%), Takotsubo CMP (8.9%), tachyarrhythmia-related chest pain (6.7%), and non-cardiac pain (9.6%). In our study, there were limitations in determining the final diagnosis and etiological factors, since the etiology research could not be performed in all aspects in our hospital. In our study, there were 99 (46.5%) patients who could be diagnosed or whose underlying cause could be partially explained. In these patients, the diagnoses were tachy-bradyarrhythmia-related chest pain (22%), heart valve pathologies (22%), Takotsuba CMP (5%), and CMP (9%) and were generally consistent with the literature.

When we look at the studies analyzing the prognosis of patients with MINOCA, they are quite heterogeneous in terms of follow-up times, cardiac mortality, and recurrent AMI. In studies, 12-month mortality rates ranged from approximately 1% in-hospital to a total of 1.2-4.7% (12-14,22). In our study, the in-hospital mortality was 1.4% for MINOCA cases, whereas the 1-year mortality was 5.6%, which was consistent with the literature.

## **Study Limitations**

The AHA and ESC guidelines differ in including certain diagnoses, such as Takotsubo syndrome, in MINOCA. In our study, we evaluated these diagnoses under the MINOCA sub-title as included in the ESC guidelines.

The cases included in our study belonged to the 1-year crosssectional period and were retrospectively included. In the evaluation, using the Hospital Information Management System retrospectively for some patients and obtaining information by interviewing their families (on the phone) for some patients can be considered as a limitation.

In our hospital, CAG is not applied to all patients who meet the definition of NSTEMI. Only those with a high probability of obstructive CAD were selected, and patients without traditional cardiovascular risk factors but with a high probability of MINOCA, such as younger patients and female patients, may not have undergone CAG. This may affect the prevalence of MINOCA.

Etiology research is not conducted in our hospital.

# Conclusion

Considering the 14% mortality and unexpected cardiac event rates reported in the literature, the etiology of MINOCA cases needs to be clarified. Risk factors for these cases should be determined, and separate risk scoring systems should be established. Thus, the treatment of cases can be organized effectively and unnecessary interventions can be prevented.

### **Ethics**

**Ethics Committee Approval:** The study was approved by the Antalya Training and Research Hospital of Ethics Committee (decision no: 1/3, date: 11.01.2018).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

## **Authorship Contributions**

Surgical and Medical Practices: A.K., E.K., Concept: A.K., F.Y., M.K., Design: E.K., M.K., Data Collection or Processing: A.K., Analysis or Interpretation: F.Y., Literature Search: A.K., M.K., R.N.O., Writing: A.K., E.K., M.K., R.N.O. **Conflict of Interest:** No conflict of interest was declared by the authors.

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# Examining the Link between the SATIS-Stroke Questionnaire and the Modified Rankin Scale in Stroke Patients at 30 Days **Post-discharge**

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## Abstract

**Original Article** 

Aim: To assess the correlation between stroke patients' satisfaction with participation and activity (measured by SATIS-Stroke) and their functional independence [measured by modified Rankin Scale, (mRS)] after 30 days of hospital discharge.

Materials and Methods: A longitudinal study was conducted on 135 stroke patients, tracking them for 1 month after stroke. Demographic data, including sex, age, marital status, education level, living conditions, and annual budget, were collected. Data analysis was performed using Statistical Package for Social Sciences version 25.0.

Results: Over the 30-day follow-up period, all 135 stroke patients completed the SATIS questionnaire and recorded mRS scores. Initially, the mean mRS score was three during hospitalization, which improved to a mean score of 2 by the end of hospitalization and follow-up. The average SATIS score was 73.

Conclusion: The SATIS questionnaire demonstrated a significant correlation with mRS, indicating its effectiveness in predicting stroke patients' clinical status and satisfaction with daily activities and lives. The study also evaluated the questionnaire's predictive value regarding age, gender, income, and marital status. Notably, the questionnaire exhibited a higher predictive value among older females and patients with higher income levels.

Keywords: SATIS-Stroke, modified Rankin Scale, stroke, International Classification of Functioning

# Introduction

Stroke is the third leading cause of functional disability and the second main cause of mortality worldwide, based on the World Health Organization (WHO) (1). The affected cases, after a stroke, may have cognitive, perceptive, motor, and sensory impairments that affect the functioning and result in disability; between 24 % and 75% of stroke survivors require outside help with their daily activities (2-4). These functional limitations directly impede activities and social involvement (5).

Based on the International Classification of Functioning (ICF), Disability and Health, participation is described (6) as the patient's participation in living circumstances. Restrictions of participation illustrate patients' problems and experiences with social role performance (e.g. worker, friend, being spouse, or parent) that are considered as usual due to their sex, age, and the culture and society in which they live. Activity is the execution of action or task by an individual. Performance and capacity are the criteria for ICF's participation and activity areas.



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Various assessment methods are used to examine the concepts of participation and activity. Both performance-based and capacitybased instruments can be used to evaluate the activity of ICF components. Usually, the measurement of capacity requires a clinical setting. Although it only sometimes needs a considerable amount of time and cost, the evaluator's training is usually required prior. Generally, performance-based instruments are administered outside of a clinical setting and tend to be questionnaires, which are time-consuming and often require specialized expertize on the part of the evaluator (7,8).

The modified Rankin Scale (mRS) is a scale of global disability with a focus on mobility to assess the functional independence level for stroke cases (9). It has been widely utilized in stroke trials as an outcome and premorbid ability measure. It has seven grades between 0 and 6, with 0 indicating no symptoms and 6 indicating death. The reliability and validity of mRS in cases of stroke as a global disability clinician-reported measure in the literature have been contentious (10-12).

The SATIS-Stroke questionnaire was established as a participation and activity satisfaction measure of stroke cases in real-life environments. Based on the Rasch measurement model, the SATIS-Stroke scores have been transformed into linear and unidimensional satisfaction measures (13,14). Additionally, it is the only scale that addresses all nine ICF domains, the participation and activity component (15,16). Consequently, SATIS-Stroke contains fields that are not contained by other scales, including applying knowledge, general tasks and demands, and learning (7,8,17).

Hence, the aim of this study was to evaluate the correlation between SATIS-Stroke score and mRS 30 days after discharge in stroke patients.

# **Materials and Methods**

### Patients

This longitudinal study collected data from Tabriz University Hospital between March 2019 and March 2022. After the study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences (ethical code: IR.TBZMED. REC.1401.515, date: 12.09.2022), informed consent was obtained from all participants. After enrollment in the study, patients were followed up for 30 days after discharge. According to the WHO criteria, stroke was characterized in this study as "developing clinical signs of global or focal cerebral function impairment rapidly, persisting for more than 24 h or resulting in death, with no known reason other than a vascular origin" (18). Patients were included in the study if (i) were older than 18 years, (ii) were diagnosed with stroke, and (iii) were admitted to the stroke ward. Patients were excluded if (i) another diagnosis was made during admission, (ii) incomplete filling of the questionnaire, and (iii) they had mental disorders and were taking medications related to them. The participants' flow chart is shown in Figure 1.

## Sample Size

Following the quality criteria guidelines for addressing the health status of questionnaires (19), it was revealed that at least 50 individuals are required for reliability analysis. Nevertheless, considering the sample features studied, we adopted Hobart et al. (20) recommendations, who recommended an adequate analysis of at least 80 participants of the measurement characteristics of testing equipment for neurological disease patients.

## Procedure

Based on the patient follow-up chart, 268 patients were initially examined. Of these, 96 patients were excluded from the study because of death. Among the remaining 172 patients, 24 were excluded because of unwillingness to follow up, and two were excluded because of incomplete questionnaires. After excluding these patients, 146 patients remained. However, for 11 of these patients, the follow-up mRS score needed to be calculated, which



**Figure 1.** Patient flow chart mRS: modified Rankin Scale

resulted in their exclusion from the study. Finally, 135 patients completed the SATIS questionnaire, and their mRS score was known during their follow-up, making them eligible for inclusion in the study. A total of 135 stroke cases were followed for one month following the onset of stroke. Each patient received instructions on how to complete the questionnaire, and each was tested individually in a quiet setting. mRS (21) was applied to assess the degree of disability on the first and last day of admission and the 30<sup>th</sup> day after discharge. SATIS-Stroke (14) was also measured on the 30<sup>th</sup> day after discharge. mRS was used as a criterion for the SATIS-Stroke questionnaire.

SATIS-Stroke is a functional assessment tool designed to assess stroke patients' level of satisfaction with their activities and participation in treatment. It provides clinicians with valuable goal-setting guidelines for effective treatment planning. With its suitable range and precise measurement capabilities, SATIS-Stroke is well suited for clinical practice (14).

## Data Collection

Demographic data included sex, age (<65,  $\geq$ 65), marital status, education level, living conditions, and annual budget. Disease variables included pathological side and subtype of stroke.

## **Statistical Analysis**

Data analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 25.0 for Windows (SPSS Inc., IL, USA). Data distribution was used to test normality using the Kolmogorov-Smirnov test. Continuous variables were displayed as mean±standard deviation (SD) or median+interquartile range (IQR): 25-75%, and categorical variables were expressed as absolute and relative frequencies (%). Because of the non-normal distribution of the variables, the non-parametric Spearman test was used to measure correlations. Where applicable, a multivariate regression analysis was conducted. Statistical significance was defined as a p value <0.05.

# Results

In total, 135 registered stroke patients completed the SATIS questionnaire with recorded mRS scores during their 30-day follow-up. There were 72 (53.3%) males and 63 (46.7%) females with a mean ( $\pm$ SD) age of 63.33 years ( $\pm$ 14.41). Ninety-two cases (68.1%) were urban and 41 (30.4%) were rural. Most individuals in this study were married (122 people); 5 (3.7%) of the patients were single. Ninety-five (70.4%) and 40 (29.6%) cases had an ischemic and hemorrhagic stroke, respectively. All participants' baseline characteristics are shown in Table 1.

The mean mRS score at the beginning of hospitalization was 3. In comparison, the mean score of mRS at the end of hospitalization

and during follow-up was 2. The mean case SATIS score was 73. Table 2 illustrates the recorded mRS grades and SATIS scores of all participants.

Spearman correlations of the SATIS-Stroke questionnaire, mRS, age (<65,  $\geq$ 65), sex, marital status, and annual budget were quantified. The results revealed that the Spearman's rank correlation coefficient (rs) was -0.765 (p<0.001) between the SATIS-Stroke questionnaire and mRS, and in Table 3, Spearman correlations between the SATIS-Stroke questionnaire and other mentioned demographic data are shown. The multiple regression analyzes of mRS, age (<65,  $\geq$ 65), sex, marital status, and annual budget for association with the SATIS-Stroke questionnaire score are shown in Table 3.

# Discussion

Stroke remains a public health challenge that results in disability in survivors, which then places a heavy financial burden on the healthcare system (22). This issue places great importance on public health agenda systems and is considered a vital area for public health research (23). Although there is no definitive method to check the severity of stroke in patients, several

Table 1. Demographic data and clinical characteristics of the135 patients			
Characteristics (n=135)	Statistics		
Age (mean±SD, years)	63.33±14.41		
Gender (n, %) Male Female	72 (53.3%) 63 (46.7%)		
Residence (n, %) Urban Rural Unknown	92 (68.1%) 41 (30.4%) 2 (1.5%)		
Marital status (n, %) Single Married Unknown	5 (3.7%) 122 (90.4%) 8 (5.9%)		
Annual income (n, %) Low Moderate High	51 (37.8%) 67 (49.6%) 17 (12.6%)		
Involved side of the brain (n, %) Right Left	72 (53.33%) 63 (46.7%)		
Type of stroke (n, %) Ischemic Hemorrhagic	95 (70.4%) 40 (29.6%)		
Patient outcome at discharge (n, %) Partial recovery Morbidity	55 (40.8%) 80 (59.2%)		
Duration of hospitalization (M, IQR, days)	9 (10)		
SD: Standard deviation, M: Median, IQR: Interquartile range			

methods have been developed for this purpose. The SATIS guestionnaire, for the first time by Bouffioulx et al. (14) in 2008, was used to evaluate the level of satisfaction of stroke patients with the quality of life, activity, and participation in daily life events. Dr. John Rankin presented a scale in 1957 that is currently used to assess the outcome of acute stroke patients after being slightly modified (24).

Ageing is the leading risk factor for stroke, which is a nonmodifiable risk and doubles every ten years after age 55. Strokes commonly occur in people over 65 years of age, accounting for almost three-quarters of all strokes. There is a predicted increase in the number of people over 65, and the number of strokes in the elderly is expected to increase, creating significant challenges for clinicians and policymakers in the foreseeable future (25).

In our study, several demographic and clinical characteristics of the participants were observed. The study sample consisted of more men than women, and most patients resided in urban

Table 2. The recorded modified Rankin Scale grades and SATIS scores of patients					
Parameter	Median	IQR			
mRS Beginning of hospitalization mRS End of hospitalization mRS 30-day mRS	3 (1-5) 2 (0-4) 2 (0-6)	2 2 2			
SATIS     73 (0-108)     72					
mRS: modified Rankin Scale, IOR: Interguartile	range				

Table 3. The Spearman correlations and multiple regression analyses between the SATIS-Stroke questionnaire, mRS and age (<65, ≥65), sex, marital status, and annual budget

Variable	rs	p value
mRS	-0.765	< 0.001
Age	·	
<65	-0.0623	< 0.001
≥65	-0.0810	< 0.001
Gender		
Male	-0.730	< 0.001
Female	-0.803	< 0.001
Marital status		· ·
Single	-0.765	< 0.001
Married	-0.763	< 0.001
Annual budget		
Low	-0.849	< 0.001
Moderate	-0.669	< 0.001
High	-0.902	< 0.001
mRS: modified Rankin Scale, rs: S	pearman's rank correlation coeffi	cient

areas. Furthermore, a significant proportion of the patients were married. The average annual income was the highest among the studied patients. In the United States, 795,000 strokes occur each year, of which 87% are classified as ischemic strokes (26).

Our study found a decrease in stroke symptom severity over time, with an average mRS score of 3 at admission and two at discharge/follow-up. A strong correlation was observed between SATIS and mRS scores, indicating that higher mRS scores were associated with lower SATIS questionnaire scores. Gender and income influenced this association. This is the first article that compares SATIS-Stroke and mRS scores at the same time. In comparison, the other articles that will be mentioned have examined each of them individually. All the information above is shown in Table 4.

One of the essential factors for stroke care, outcomes, and risk is socioeconomic status. Socioeconomic status is characterized by a person's social and economic association with others and is usually assessed by income, occupation, and education (27). A study revealed that approximately 30% of the heightened risk of severe stroke in low socioeconomic status patients could be attributed to differences in risk factors. In contrast, the impact of stroke prevention drugs was minimal. This emphasizes the need for clinicians to prioritize aggressive management of risk factors in individuals with lower education levels to reduce stroke severity. Furthermore, the study advocates for the broader adoption of mediation analysis to better understand the intricate connections between socioeconomic status and health outcomes (28). As our study evaluated the relationship between economic

Table 4. Multiple regression analyses between the SATIS-Stroke questionnaire, mRS and age (<65, ≥65), sex, marital status, and annual budget

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Parameter	CI 95%	Beta	p value					
mRS	[-19.7, -14.7]	-17.2	< 0.001					
Age								
<65	[-16.7, -8.8]	-12.8	< 0.001					
≥65	[-21.5,-14.9]	-18.22	< 0.001					
Gender								
Male	[-20, -12.7]	-16.4	< 0.001					
Female	[-21.4, -14.6]	-18	< 0.001					
Marital status								
Single	[-63.1, 13.5]	-24.7	0.132					
Married	[-19.4, -14.2]	-16.84	< 0.001					
Annual budget								
Low	[-22.2, -15.5]	18.9	< 0.001					
Moderate	[-19.4, -11.0]	15.2	< 0.001					
High	[-27.4, -15.9]	21.6	< 0.001					
mRS: modified Rankin Scale, CI: Confidence interval								

factors and stroke severity, the results from both articles were consistent with each other.

In ElHabr et al. (29), it was observed that the discharge mRS scores of stroke patients remained consistent for the first month. However, within 30 to 90 days post-discharge, approximately two-thirds of patients experienced a significant change in their mRS scores, with approximately one-third showing an improvement, deterioration, or no change. Our research also revealed similar findings, with the median and IQR of mRS scores during discharge and follow-up on the 30<sup>th</sup> day consistent with ElHabr et al.'s (29) study, but without measuring SATIS-Stroke scores. Notably, ElHabr et al.'s (29) study also evaluated mRS scores on the 90<sup>th</sup> day. These results suggest that long-term monitoring is crucial for assessing the recovery trajectory of stroke patients after hospital discharge.

In the study by Pereira et al. (30) in 2021 in Brazil, the clinical characteristics of the SATIS-Stroke questionnaire were evaluated in the population of Brazil. In this study, 80% of stroke survivors were examined. The mean age was  $57/98\pm13/85$  years. Good reliability was obtained from this questionnaire. In concurrent validity analysis, a positive, strong, and notable association was found between stroke-specific life scale quality and SATIS-Strokescores. Diagnostic accuracy was revealed with a sensitivity of 80.8% and specificity of 85.2%. This study showed that the Brazilian version of the SATIS-Stroke questionnaire has reasonable diagnostic accuracy, concurrent validity, and adequate reliability.

Banks and Marotta (11) examined the validity and reliability of mRS in stroke cases, among other studies. Several studies have reported the construct validity of mRS based on its association with physiological factors such as perfusion, lesion size, a type of stroke, and neurological disorders. It is well documented that the mRS and other disability scales have convergent validity. Patients' comorbidities and socioeconomic factors should be considered in the correct application and interpretation of mRS (11).

### Study Limitations

There are limitations to our data that must be considered when interpreting our results; we could not communicate with Wernicke aphasia patients; therefore, we could not include this group of patients in the study. In addition, more research for a higher level of data granularity with a greater sample size is required, which could reveal the correlation between the SATIS questionnaire and other factors.

## Conclusion

In conclusion, this study demonstrated a strong correlation between the SATIS questionnaire and the mRS in assessing follow-up stroke patients' clinical status and satisfaction. The results indicated that the SATIS questionnaire could effectively predict patients' functional outcomes and overall quality of life. Moreover, the analysis of demographic factors revealed that the predictive value of the questionnaire was exceptionally high among older patients, females, and those with higher income levels. These findings highlight the importance of incorporating the SATIS questionnaire as a valuable tool for evaluating stroke patients' recovery and satisfaction with life and daily activities.

#### Ethics

**Ethics Committee Approval:** The study was approved by the Tabriz University of Medical Sciences of Ethics Committee (ethical code: IR.TBZMED.REC.1401.515, date: 12.09.2022).

**Informed Consent:** Written informed consent was obtained from the patient to publish this study.

Peer-review: Externally peer-reviewed.

## **Authorship Contributions**

Surgical and Medical Practices: A.A., Concept: S.S.V., Design: S.S.V., Data Collection or Processing: A.R., Analysis or Interpretation: N.G., Literature Search: F.O., M.M., Writing: A.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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**Original Article** 

# Evaluation of the Effect of COVID-19 on Pulmonary Artery and Aortic Diameter and the Relationship Between These Vessels and Lung Volume

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## Abstract

**Aim:** Coronavirus disease-2019 (COVID-19) has primarily affected the respiratory system since its first emergence in China. Therefore, we aimed to evaluate the possible effects of this disease on pulmonary vessels and aortic diameter and the relationship between these vessels and lung volumes as it affects lung capacity.

**Materials and Methods:** In our study, the diameter of the pulmonary trunk (PT) at its origin and at the point where it divides into two, the diameters of the right and left pulmonary arteries, the diameters of the ascending aorta, aortic arch, descending aorta, and lung volumes were evaluated. Computed tomography (CT) images of 30 patients (18 men, 12 women) were obtained retrospectively, and the first measurement was performed on thorax CT images at Stage 1 (days 0-4) and the second measurement was performed on thorax CT images at Stage 6 (>day 28).

**Results:** We found a statistically significant difference in pulmonary artery and aortic diameters between Stage 1 and Stage 6 images due to the progression of COVID-19 disease (p<0.05). The difference between Stages 1 and 6 was higher in older individuals. A statistically significant difference was found between lung volumes and the PT.

**Conclusion:** We found that COVID-19 disease caused an increase in the pulmonary artery and aortic diameter due to its poor prognosis, and there was a significant relationship between lung volume and pulmonary vessels.

Keywords: COVID-19, diameter, pulmonary trunk, aorta

# Introduction

Coronavirus disease (COVID-19), which originated in China, started in early 2020 and has become a highly virulent pandemic. COVID-19 is a highly contagious disease that mainly causes acute respiratory distress syndrome (ARDS), vascular damage, microangiopathy, angiogenesis, and disseminated thrombosis. Common symptoms include fever, cough, fatigue, and shortness of breath (1,2). Patients may have an asymptomatic stage following infection or only mild upper respiratory symptoms may be observed. In addition, pneumonia and severe ARDS requiring intubation develop, and complications resulting in death occur. In the later stages of the disease, a worsening clinical scenario occurs with the development of severe pulmonary lesions leading to vascular thrombosis and pulmonary arterial and venous vasculopathy, as well as disseminated intravascular coagulation (3,4).

Distinctive features of COVID-19 include vascular changes associated with the disease. Diffuse intravascular coagulation and multisystem organ failure have been observed in many patients. Therefore, the risk of disease-causing pneumonia and therefore death is also high (5).



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© Copyright 2023 The Emergency Physicians Association of Turkey / Eurasian Journal of Emergency Medicine published by Galenos Publishing House. Licenced by Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) 4.0 International License. COVID-19 is also likely to affect the heart and cardiac vessels, resulting in strain on lung capacity and impairment of small circulation. Possible cardiac damage includes increased cardiac stress due to respiratory failure and hypoxemia, pulmonary embolism, and myocardial infection. Similar to pulmonary hypertension, pulmonary artery pressure is likely to increase following heart failure (2,3).

While the diagnosis of COVID-19 is determined by polymerase chain reaction, computed tomography (CT) is used for the rapid diagnosis of COVID-19 and determination of lung involvement, especially in emergency departments. Therefore, CT has an essential role in the early diagnosis of COVID-19 pneumonia, and pathophysiological vascular changes in patients affected by COVID-19 can be easily detected by CT (3,5). Diffuse lung consolidation and ARDS that develop with the disease may lead to pulmonary hypertension by changing the properties of pulmonary vessels (6).

Pulmonary hypertension is a term used to describe disorders characterized by abnormally high pressures in the pulmonary arteries. Pulmonary hypertension is rarely caused by chronic thromboembolism or primary vasculopathy (7,8). Similar to pulmonary hypertension, COVID-19 patients may have an increase in the diameter of the pulmonary arteries and a change in the diameter of the aorta and its parts due to heart failure, which may occur indirectly. Therefore, we evaluated the diameter changes in the pulmonary arteries, aorta, and its parts in COVID-19 patients.

# Materials and Methods

## Patients

The study was approved by the Ordu University Clinical Research Ethics Committee (decision no: 2023/45, date: 23.02.2023) and the Provincial Directorate of Health affiliated to the Ministry of Health. Thorax CT images of patients hospitalized with a preliminary diagnosis of COVID-19 were obtained retrospectively from the imaging system of the Training and Research Hospital. The images obtained were the first CT scan taken on days 0-4 (Stage 1) and the second CT scan taken on day >28 (Stage 6) of the patient hospitalized with the diagnosis of COVID-19. Patients without any lung or vascular pathology and those diagnosed with COVID-19 were included in the study. Patient characteristics (gender and age) and clinical diagnoses were extracted from the images. Measurements were performed on 30 patients (18 males, 12 females, mean age 54.33 years).

### **Measurements**

CT imaging was performed using a multi-detector CT scanner (Canon Aquilion Lightning Core 128, Japan). 1.5-mm-thick CT images were obtained during deep inspiration, and participants were instructed to remain in that position to minimize motion artifacts Measurements were performed on an axial thorax CT image in accordance with the standards specified in the literature using the RadiAnt Digital Imaging and Communications in Medicine (DICOM) Viewer software in Stages 1 and 6. The widest diameter of the pulmonary trunk (PT) after leaving the right ventricle (RV), the widest diameter of the PT where it splits into two (PTS), the widest diameter of the right (RPA) and left pulmonary arteries (LPA), the widest diameter of the aortic arch at its highest point, the widest diameter at the beginning of the ascending aorta, and the widest diameter of the first part of the descending aorta (thoracic aorta) were measured (Figure 1a). Lung volumes were calculated using the ImFusion Suite program. First, the "dcm2niigui" software was used to convert the original CT images in DICOM format into SPM8 (3D Niftii) format. These images were then used for lungvolume calculation using the ImFusion Suite program (Figure 1b).



Figure 1. a) Measurement of vessel diameters (A: left pulmonary artery, B: right pulmonary artery, C: aortic arch, D: ascending aorta, E: descending aorta, F: pulmonary trunk beginning). b) Measurement of lung volume using software

1a

# **Statistical Analysis**

Descriptive data are expressed as mean and standard deviation. The Shapiro-Wilk test was used to assess the distribution of continuous variables. For non-normally distributed variables, the Wilcoxon signed-rank test was used to compare the differences. Pairwise comparisons of the continuous variables between independent groups were performed using the Mann-Whitney U test. A p value of <0.05 was considered statistically significant. All statistical tests were performed using Statistical Package for the Social Sciences 28.0 software.

# Results

Thirty participants (12 females, 18 males) with a diagnosis of COVID-19 were included in our study. The average age of the participants was  $54.33\pm16.38$  (between 22 and 90 years old). The mean values of the parameters and comparisons according to gender and age were evaluated. The minimum and maximum values of the parameters in Stages 1 and 6 of COVID-19 are given in Table 1.

The vessel diameter values measured in Stage 6 were significantly increased compared with those measured in Stage 1. Except for

Table 1. The minimum and maximum values of vessels in Stage       1 and Stage 6 of COVID-19 disease							
Vessels	n	Stage 1	Stage 6				
PT, cm	30	2.80-4.56	2.85-4.75				
PTS, cm	30	2.35-4.33	2.42-4.45				
RPA, cm	30	1.57-2.97	1.58-3.17				
LPA, cm	30	1.48-2.80	1.55-2.95				
Ascending aorta, cm	30	2.47-4.55	2.51-4.80				
Aortic arch, cm	30	1.95-3.28	2.09-3.45				
Descending aorta, cm	30	1.84-3.68	1.89-3.72				
COVID-19: Coronavirus disease-2019, PT: Pulmonary trunk, LPA: Left pulmonary artery, PTS: Pulmonary trunk seperation, RPA: Right pulmonary artery							

the PTS diameter (p=0.056), we found a statistically significant difference between Stage 1 and Stage 6 (p<0.05). All parameters demonstrated a high positive correlation (Table 2).

The mean values of the parameters in Stages 1 and 6 are shown in Table 3 according to gender. Vascular diameters were higher in males than in females. However, when the parameters were compared between Stage 1 and Stage 6 according to gender, no statistically significant difference was determined except for the descending aorta and RPA (Table 4).

We evaluated the effect of age on the increase in vessel diameter in Stages 1 and 6. We found that COVID-19 caused a statistically significant increase in the diameters of LPA, RPA, aorta, and its parts in Stage 1 and Stage 6 due to aging (p<0.05). Because the prognosis of the disease is worse in elderly people, we would report that the effect on the increase in vessel diameter is greater.

The total lung volumes calculated in Stages 1 and 6 are shown in Table 5. Accordingly, right and left lung volumes decreased with the progression of COVID-19 disease. There was no statistically significant difference in lung volumes between Stage 1 and Stage 6 (p=0.125 and p=0.189). The relationship between the pulmonary artery and the right and left lung was evaluated in Stages 1 and Stage 6 and a moderate positive correlation was found, except for the relationship between the pulmonary artery and the left lung in Stage 1 (Table 5).

# Discussion

Coronavirus binds to receptors in the alveoli in the lungs, enters the cell, damage. As the disease progresses, pulmonary hemodynamics deteriorate and consolidated areas of the lungs develop. These are followed by abnormal dilation of the pulmonary vessels and a high thromboembolic risk. Therefore, lung capacity is strained, and the possibility of dilatation increases in parallel with increased pressure in the pulmonary

Table 2. Changes in pulmonary vessels and aortic diameter in Stage 1 and Stage 6 of COVID-19 disease and statistical analysis									
Vessels	n	Stage 1	Stage 6	р	r	Test			
PT, cm	30	3.64±0.44	3.85±0.48	<0.001	0.772	**			
PTS, cm	30	2.96 (2.35-4.33)	3.03 (2.42-4.45)	0.056	0.901	*			
RPA, cm	30	2.15±0.31	2.22±0.33	0.017	0.913	**			
LPA, cm	30	2.06±0.30	2.14±0.33	0.001	0.940	**			
Ascending aorta, cm	30	3.50±0.51	3.59±0.55	<0.001	0.987	**			
Aortic arch, cm	30	2.66±0.38	2.78±0.39	<0.001	0.981	**			
Descending aorta, cm	30	2.59±0.41	2.67±0.43	0.002	0.958	**			

\*Spearman's Rho correlation, \*\*Pearson correlation, r: Correlation coefficient, p: Significance values (p<0.05 indicates significant difference). The non-parametric data are presented as median (minimum-maximum). The parametric data are presented as mean±standard deviation. COVID-19: Coronavirus disease-2019, PT: Pulmonary trunk, LPA: Left pulmonary artery, PTS: Pulmonary trunk seperation, RPA: Right pulmonary artery

vessels and indirectly in the aorta. The pulmonary artery diameter may also increase in pathological conditions such as pulmonary hypertension and RV enlargement (2,6,9).

The identified cardiac effects of COVID-19 include myocarditis, myocardial infarction, heart failure, and RV dysfunction. Studies have shown that RV dysfunction occurs in 20-40% of patients with ARDS and lung damage. RV enlargement and pulmonary artery dilatation affect each other. Because of lung injury and vascular inflammation, the load of the RV increases; therefore, an increase in diameter may develop with an increase in pulmonary artery pressure (10,11). Therefore, in our study, we have evaluated all of these issues, which are missing in the literature, on a large scale. In COVID-19 disease, we found a significant increase in PT, RPA, LPA, and diameters of the aorta and its parts and a statistically significant difference in Stage 1 and Stage 6 COVID-19 CT images. We also observed that this statistical difference increased with age. We evaluated the relationship between lung volume and pulmonary vessels and the aorta and its parts and found a positive correlation.

Spagnolo et al. (6), in their study evaluating PT and aortic diameter in patients with COVID-19, measured a mean PT diameter of 31 mm and found a statistically significant difference between PT and aorta and showed that PT diameter increase was associated with the risk of death in patients with patients. In another study, PT and its branches were evaluated on CT images of patients with pulmonary hypertension, and an increase in the diameter of

Table 3. Evaluation of pulmonary vessels and aortic diameters according to gender and statistical analysis						
Vessels	Men (n=18)	Women (n=12)	р			
	Stage 1 - Stage 6	Stage 1 - Stage 6	Stage 1 - Stage 6			
PT, cm	3.72±0.48 - 3.96±0.50	3.52±0.36 - 3.69±0.41	0.241* - 0.125*			
PTS, cm	3.05-3.09	2.80-2.87	0.205** - 0.086**			
RPA, cm	2.25±0.35 - 2.29±0.40	2.00±0.16 - 2.10±0.15	0.031* - 0.123*			
LPA, cm	2.15±0.35 - 2.22±0.37	1.93±0.14 - 2.03±0.24	0.051* - 0.140*			
Ascending aorta, cm	3.54±0.52 - 3.65±0.58	3.43±0.51 - 3.50±0.50	0.578* - 0.494*			
Aortic arch, cm	2.74±0.39 - 2.86±0.41	2.55±0.35 - 2.65±0.33	0.170* - 0.154*			
Descending aorta, cm	2.75±0.41 - 2.83±0.43	2.36±0.28 - 2.44±0.35	0.010* - 0.017*			

p: Significance value between men and women in Stage 1 and Stage 6 (p<0.05 indicates significant difference).

All parametric data are presented as mean±standard deviation. Independent samples t-test was applied for gender comparison in parametric data\*.

All non-parametric data are presented as median. Mann-Whitney U test was applied for gender comparison in non-parametric data\*\*.

COVID-19: Coronavirus disease-2019, PT: Pulmonary trunk, LPA: Left pulmonary artery, PTS: Pulmonary trunk seperation, RPA: Right pulmonary artery

#### Table 4. The effect of age on changes in aorta and pulmonary vessels in COVID-19 disease

	Stage 1 - Stage 6						
	PT*	PTS**	RPA*	LPA*	Ascending aorta*	Aortic arch*	Descending aorta*
r	-0.102	0.238	0.466	0.469	0.749	0.723	0.697
	0.021	0.270	0.385	0.547	0.712	0.706	0.706
р	0.590	0.206	0.009	0.009	<0.001	<0.001	<0.001
	0.912	0.149	0.036	0.002	<0.001	<0.001	<0.001

p: Significance value (p<0.05 indicates significant difference), r: Correlation coefficient.

Pearson correlation coefficient\* was used to show age-related change in parametric data and Spearman's correlation coefficient\*\* was used in non-parametric data. COVID-19: Coronavirus disease-2019, PT: Pulmonary trunk, LPA: Left pulmonary artery, PTS: Pulmonary trunk seperation, RPA: Right pulmonary artery

Table 5. Lung volumes measured at Stage 1 and Stage 6 in COVID-19 patients and correlation of pulmonary trunk with lung volumes							
	n	Right lung (cm <sup>3</sup> )	Pearson correlation coefficient (PT)	Left lung (cm <sup>3</sup> )	Pearson correlation coefficient (PT)		
Stage 1	30	2369.00±798	p=0.013** r=0.490	2095.00±696	p=0.065 r=0.375		
Stage 6	30	2187.00±765	p=0.008** r=0.517	1958.00±779	p=0.021** r=0.459		
p*		0.125		0.189			

p\*: Significance value between right and left lung in Stage 1 and Stage 6. p\*\*: Significance value between lung volume and pulmonary trunk, r: Pearson correlation coefficient. All parametric data are presented as mean±standard deviation.

COVID-19: Coronavirus disease-2019, PT: Pulmonary trunk

these vessels was demonstrated (7). In our study, the PT diameter was calculated as 3.64 cm in Stage 1 and the PTS diameter was found to be 2.96 cm on average.

As we found in our study, the relationship between PT diameter and COVID-19 disease has been observed similarly in men and women in other studies (6). A statistically significant difference was found between genders, especially in the diameter of the descending aorta in Stage 1 and Stage 6.

Pulmonary hypertension is one of the pathologies in which PT diameter is of most importance, and there is a large body of literature demonstrating that main pulmonary artery diameter exceeding 29 mm by contrast-enhanced CT is a marker of pulmonary hypertension (7). In our measurements, PT (2.80-4.75) and PTS diameter (2.35-4.33) were found in a wide range due to the wide age range (22-90 years).

Lung volume measured on CT images is closely related to pulmonary function test results (12). Decreased lung volume may be an important sign of COVID-19 infection and prognosis of ARDS. Studies have reported that lung volume reduction detected on CT in COVID-19 cases is associated with more alveolar collapse (13,14). However, in our study, we did not detect a significant decrease in lung volume between Stages 1 and 6. The reason for the lack of a significant lung volume difference may be that lung involvement improves until Stage 6 of the disease or the most severe level of the disease develops after the first 10 days (15).

### Study Limitations

The limitation of the study presented here is that the images could not be obtained easily due to the pandemic situation; therefore, the number of patients was low.

## Conclusion

In conclusion, COVID-19 directly affects the lungs and indirectly affects the vessels that supply the lungs. We found a statistically significant abnormal vasodilatation in the pulmonary arteries in Stage 6 with COVID-19-induced lung dysfunction and a severe prognosis of the disease. We found that this dilatation is more effective, especially in elderly individuals. RV enlargement may develop with abnormal dilatation of the pulmonary arteries. Therefore, when we examined the aorta and its branches originating from the heart, we found a statistically significant increase between Stages 1 and 6. We found that gender had no effect on the development of pulmonary arteries due to COVID-19 disease. We also found a moderate positive correlation between total lung volume and pulmonary artery diameter. Based on these results, we suggest that COVID-19 disease adversely affects the lungs, pulmonary vessels, and aorta.

## Ethics

**Ethics Committee Approval:** The study was approved by the Ordu University Clinical Research Ethics Committee (decision no: 2023/45, date: 23.02.2023) and the Provincial Directorate of Health affiliated to the Ministry of Health.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

#### **Authorship Contributions**

Surgical and Medical Practices: M.D., Concept: M.D., İ.U., M.S.C., Design: M.D., İ.U., M.S.C., Ş.T.S., Data Collection or Processing: M.D., Ş.T.S., A.A., Analysis or Interpretation: M.D., Literature Search: M.D., Writing: M.D.

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# Prognostic Utility of the Ratio of Pulmonary Artery Diameter to Ascending Aorta Diameter in COVID-19 Patients

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# Abstract

**Aim:** Numerous hospital admissions of patients infected with Coronavirus disease-2019 (COVID-19) reveal the importance of managing clinical, radiological, and laboratory findings related to disease severity and mortality. Pulmonary artery (PA) trunk enlargement is a well-known indicator of hemodynamic instability. The purpose of this study was to assess the prognostic value of PA trunk diameter enlargement and the ratio of the PA diameter to the ascending aorta (AA) diameter on unenhanced computed tomography images in patients with severe COVID-19 infection.

**Materials and Methods:** Three hundred and ninety-three hospitalized patients in the pandemic ambulatory service, emergency department, and intensive care unit were retrospectively analyzed. Correlations between the PA diameter and the ratio of the PA diameter to the AA diameter with prognostic factors and values were examined.

**Results:** PA/AA rates were significantly higher in hospitalized patients who developed mortality. The optimum cut-off PA/AA ratio to predict mortality was 0.9386, with a sensitivity of 98% and specificity of 97%. The optimum cut-off PA diameter to predict mortality was 3.315 cm, with a sensitivity of 98% and specificity of 89%. The mortality risk was 221 times higher in patients with a PA/AA ratio higher than 0.93 and 65 times higher in patients with a PA diameter greater than 3.315 cm.

**Conclusion:** PA trunk diameter enlargement and the PA/AA diameter ratio can be valuable markers for predicting the mortality risk of COVID-19.

Keywords: Pulmonary artery diameter, ascending aorta diameter, COVID-19

# Introduction

Viral transmission has increased because of asymptomatic infections, limited testing, and inadequate personal protective equipment for healthcare providers worldwide (1). A new infection caused by Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2), named Coronavirus disease-2019 (COVID-19), has affected healthcare systems and communities. The numerous hospital admissions of patients infected with COVID-19 reveals the importance of managing clinical, radiological, and laboratory findings related to disease severity and mortality. Identifying potential risk factors that predict disease progression will help healthcare professionals triage patients effectively, personalize treatment, monitor clinical progress, and allocate appropriate resources at all levels of care to reduce morbidity and mortality (2).

A very high number of admissions to health centers or hospitals during an epidemic is essential (3). This high demand, especially the need for intensive care support, overwhelms human and mechanical capacities (4). An academician of the American Society for Radiation Oncology called for the immediate establishment of a computed tomography (CT)based diagnostic method for COVID-19 and improvement of the detection rate of SARS-CoV-2 (5). In such an environment, another solution with sufficient accuracy is needed to guide the rapid management of patients admitted to the hospital during this pandemic. Therefore, early and effective predictors



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© Copyright 2023 The Emergency Physicians Association of Turkey / Eurasian Journal of Emergency Medicine published by Galenos Publishing House Licenced by Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) 4.0 International License. of clinical outcomes are urgently needed for risk stratification of COVID-19 patients.

The advantages of CT in diagnosing COVID-19 are clear because this method has great value for early screening, differential diagnosis, and assessment of disease severity (6). Although the virus prefers the lungs, the infection also severely affects the whole body and cardiovascular system (7). Pulmonary artery (PA) trunk enlargement is a well-known indicator of hemodynamic instability, such as acute central pulmonary embolism and heart failure (8,9). Enlargement of the PA body likely reflects cardiovascular injury, intrapulmonary inflammation, and abnormal blood coagulation. However, the prognostic value of this parameter and the optimal cut of the PA trunk diameter for predicting mortality on non-contrast CT images have not been well evaluated. The aim of this study was to investigate whether the ratio of PA diameter measured on CT imaging and PA diameter to ascending aorta (AA) diameter has a prognostic value in COVID-19 patients.

# **Materials and Methods**

## Study Design and Patient Population

This was a retrospective study conducted at the Department of Emergency Medicine, Ufuk University Faculty of Medicine. The study included 393 hospitalized COVID-19 patients in the pandemic service, emergency department, and intensive care unit (ICU) of Ufuk University Medical Faculty Dr. Ridvan Ege Hospital, a tertiary reference center in Ankara, between 11.03.2020 and 24.03.2022. The Ufuk University Hospital Ethics Committee and the Ministry of Health approved the study protocol (decision no: 22.05.12.05/07, date: 12.05.2022). The inclusion criteria were hospitalized adult patients (aged 18 years or older) with laboratory (COVID-19-PCR)-confirmed COVID-19 who underwent at least one chest CT scan. Patients below 18 years of age, patients without CT imaging, patients with pulmonary hypertension, those with negative COVID-19-PCR results, and pregnant and non-hospitalized patients were not included. Patients with missing data were also excluded from the study.

All procedures applied in this study agreed with the Declaration of Helsinki. Clinical data of patients, length and type of hospital stay, and discharge status were obtained from the hospital registry database.

## Measurements

The patient's laboratory parameters and chest CT findings were recorded. Blood samples included white blood cell (WBC), lymphocytes, neutrophils, C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), and ferritin. PA diameter, AA diameter, and PA/AA ratio were recorded using CT scans. PA diameter, AA diameter, and the ratio of PA diameter to AA diameter were measured at the level of the PA bifurcation in the axial plane using computerized chest tomography. Correlations between the PA diameter and the ratio of the PA diameter to the AA diameter with prognostic factors and values were examined (Figure 1).

## **Statistical Analysis**

All statistical analyzes were performed using Statistical Package for the Social Sciences 22. The Kolmogorov-Smirnov test was applied as the normal distribution test. Parametric tests were used in the analysis of normally distributed data, and non-parametric tests were used when data were not normally distributed. The Mann-Whitney U test, t-test, binary logistic regression analysis, Spearman correlation analysis, and ROC analysis were used for statistical analyzes A p value of <0.05 is considered statistically significant.

# Results

Our study's mean age of 393 patients was  $66.81\pm14.89$  (minimum: 20-maximum: 99). The baseline demographic, clinical features, and comorbidities of the COVID-19 patients are given in Table 1.



**Figure 1.** Axial images of non-contrast chest computed tomography demonstrating measurement of lung involvement due to Coronavirus disease-2019 and the corresponding pulmonary image in the parenchyma window. Increased pulmonary artery/ ascending aorta (PA/AA) ratio was associated with the severity of lung involvement. The PA/AA ratios were 0.6-0.98-1.17, respectively

There was a statistically significant difference in laboratory parameters and the ratio of PA diameter to AA diameter according to the ICU requirement of patients. WBC, neutrophil, CRP, D-dimer, LDH, ferritin levels, and PA/AA ratios were statistically significantly higher in the ICU (Table 2).

There was a statistically significant difference in laboratory parameters and the ratio of PA diameter to AA diameter according to in-hospital mortality status. WBC count, neutrophil count, CRP, D-dimer count, LDH, ferritin level, and PA/AA ratio were statistically significantly higher in the non-survivor group compared to the survivor group (Table 3).

There was a weak negative correlation with the PA/AA ratio with lymphocytes and a weak positive correlation with WBC, neutrophils, CRP, D-dimer, LDH, and ferritin (Table 4).

Considering the usability of PA/AA ratio and PA diameter to discriminate between patients' mortality at the time of admission, the area under the curve was found to be 0.997 for PA/AA ratio and 0.974 for PA diameter. PA/AA ratio and PA diameter can be diagnostic markers for predicting the mortality risk for COVID-19 patients (Figure 2, Table 5).

The optimum cut-off PA/AA ratio to predict mortality was 0.9386 with a sensitivity of 98%, specificity of 97%, and Youden's J index

Table 1. Demographics, clinical features, and comorbidities of Coronavirus disease-2019 patients					
Baseline features	n=393	%			
Gender (male)	214	54.5			
Gender (female)	179	45.5			
Hypertension	194	49.4			
Diabetes mellitus	112	28.5			
Coronary artery disease	86	21.9			
Chronic obstructive pulmonary disease	66	16.8			
Congestive heart failure	41	10.4			
Asthma	33	8.4			
Cancer	26	6.6			
Cerebrovascular disease	13	3.3			
Clinical features					
Dyspnea	223	56.7			
Cough	168	42.7			
Fever (temperature ≥37.3 °C)	146	37.2			
Myalgia or fatigue	104	26.5			
Sore throat	33	8.4			
Headache	17	4.3			
Diarrhoea	10	2.5			
Loss of taste	3	0.8			
Anosmia	2	0.5			

of 0.95. The positive likelihood ratio (true positive/false positive ratio) was 33.7 and the negative likelihood ratio (true negative/ false negative) was 0.02. These results show that the PA/AA ratio is a near-perfect diagnostic test for predicting mortality. The optimum cut-off PA diameter to predict mortality was 3.315 cm, with a sensitivity of 98% and specificity of 89%. Youden's J index was 0.87. The positive likelihood ratio (true positive/false positive ratio) was 9.33 and the negative likelihood ratio (true negative/ false negative) was 0.02. These results indicate that PA diameter is a significant predictor of subsequent death (Table 6).

The logistic regression analysis for predicting mortality was valuable (Omnibus test p<0.001). The independent predictors in the model determine 89.3% of the change in the dependent predictors. The accuracy rate of the model was 97.5%. The dependent variables of the model were mortality status and the independent variables were CRP, D-dimer, LDH, ferritin, PA diameter, and PA/AA ratio. The PA/AA ratio is divided into two categories according to the recommended cutoff value. Values above 0.9386 were considered risky. The PA diameter is divided into two categories according to the recommended cut-off value. Values above 3.315 cm are considered risky. The mortality risk was 221 times higher in patients with a PA/AA ratio higher than 0.93 and 65 times higher in patients with a PA diameter greater than 3.315 cm (Table 7).

## Discussion

Chest CT scanning is widely used for diagnostic and prognostic purposes in COVID-19 patients. The virus infects the lungs, affecting the whole body and especially severely affecting the cardiovascular system. PA trunk enlargement indicates



**Figure 2.** Area under the curve for PA/AA and PA AA: Ascending aorta, PA: Pulmonary artery

Table 2. Laboratory and radiographic features of COVID-19 patients in the intensive care unit and in-patients									
	Hospitalized patient (n=393)								
	Intensive ca	Intensive care unit (n=73)			In-patients (n=320)				
	Average	Standard deviation	Median	Average	Standard deviation	Median	- p		
WBC (cells/µL)	15093.56	8326.91	13600	9789.22	6330.28	8885	< 0.001		
Lymphocyte (cells/µL)	968.49	835.31	600	1602.54	1516.91	1300	< 0.001		
Neutrophile (cells/µL)	13193.01	7841.42	11500	6939.53	4391.57	6100	< 0.001		
CRP (mg/L)	137.72	92.59	121	72.51	70.34	53.95	< 0.001		
D-dimer (µg/L)	3203.58	3434.85	1550	785.13	1190.33	362.50	< 0.001		
LDH (IU/L)	463.37	257.27	407	249.48	116.32	225	< 0.001		
Ferritin (µg/L)	1062.93	698.40	890	362.76	421.23	220.50	< 0.001		
PA/AA ratio	1.00	0.08	0.98	0.78	0.07	0.78	< 0.001		
AA: Ascending porta PA: Pulmon	A): Ascending parts PA: Pulmonzy artery CPP: C reactive protein WPC: White blood cells LDH: Lactate debydrogenase COVID 10: Coronavirus disease 2010								

AA: Ascending aorta, PA: Pulmonary artery, CRP: C-reactive protein, WBC: White blood cells, LDH: Lactate dehydrogenase, COVID-19: Coronavirus disease-2019

### Table 3. Laboratory and radiographic features of COVID-19 patients according to in-hospital mortality status

	Mortality							
	Survivor (n=	Survivor (n=342)		Non-survivo	Non-survivor (n=51)			
	Average	Standard deviation	Median	Average	Standard deviation	Median	þ	
WBC (cells/µL)	9944.21	6319.29	9090	16342.35	8959.56	14030	< 0.001	
Lymphocyte (cells/µL)	1569.92	1491.21	1300	913.73	784.35	600	< 0.001	
Neutrophile (cells/µL)	7147.05	4522.28	6300	14499.02	8403.67	12400	< 0.001	
CRP (mg/L)	75.64	71.86	56.30	144.89	97.42	124.50	< 0.001	
D-dimer (µg/L)	840.49	1269.67	409.50	3875.61	3716.35	2040	< 0.001	
LDH (IU/L)	257.61	124.38	230	501.06	279.12	464	< 0.001	
Ferritin (µg/L)	395.07	468.19	230.50	1148.31	647.01	1099	< 0.001	
PA/AA ratio	0.79	0.08	0.79	1.03	0.07	1.02	< 0.001	
AA: Ascending aorta, PA: Pu	lmonary artery, C	RP: C-reactive protein, WBC:	White blood cell	s, LDH: Lactate deh	ydrogenase, COVID-19: Coronav	irus disease-2019	)	

			PA/AA ratio
Spearman's Rho	WDC	R	0.253
	WBC	Р	<0.001
	Lymphosyte	R	-0.314
	Lymphocyte	Р	<0.001
	Neutrophil	R	0.321
	Neutrophii	Р	<0.001
	CDD	R	0.240
	CKP	Р	<0.001
	D dim en	R	0.368
	D-dimer	Р	<0.001
		R	0.375
		Р	<0.001
	Forritin	R	0.326
	Fernum	Р	<0.001

hemodynamic instability, such as acute central pulmonary embolism and heart failure (8,9). The dilation of the PA trunk likely reflects cardiac and vascular injury, abnormal blood coagulation, and intrapulmonary inflammation. However, the prognostic value of this parameter and the optimal cut-off of PA trunk diameter on unenhanced CT images to predict mortality have not been well evaluated.

Our study's mean age of 393 patients was 66.81±14.89. 81.4% of the patients were hospitalized, 18.6% had intensive care admission, and 13% of the patients died after hospitalization. Puhr-Westerheide obtained different results in a group of 89 COVID-19 ICU acute respiratory distress syndrome patients requiring mechanical ventilation or continuous positive airway pressure mask ventilation. This retrospective study suggested that CT severity scores and PA-to-AA ratios were not significantly associated with in-hospital mortality (10). WBC count, neutrophil count, CRP level, D-dimer level, LDH level, ferritin level, and PA/ AA ratios were significantly higher in ICU patients and patients with mortality. There was a weak negative correlation between

PA/AA ratio and lymphocytes and a weak positive correlation between WBC, neutrophils, CRP, D-dimer, LDH, and ferritin. The optimum cut-off PA/AA ratio to predict mortality was 0.9386, with a sensitivity of 98% and specificity of 97%. The optimum cut-off PA diameter to predict mortality was 3.315 cm, with a sensitivity of 98% and specificity of 89%. It was found that the mortality risk was 221 times higher in patients with a PA/AA ratio higher than 0.93 and 65 times higher in patients with a PA diameter greater than 3.315 cm.

Main PA diameter (MPAD) enlargement is associated with pulmonary hypertension and mortality in patients without COVID-19. Esposito et al. (11) investigated the association between PA enlargement and overall survival in patients with COVID-19. A cohort study was conducted with 1.469 patients with COVID-19 who underwent chest CT within 72 h of admission to seven tertiary hospitals in Northern Italy between March 1 and April 20, 2020. Enlargement of the PA diameter (≥31 mm) was found to be a predictor of mortality. In patients with more than 31 mm PA diameter, the mortality risk was 1.592 times greater. Enlargement of MPAD (≥31 mm) was found to be an indicator of mortality in the corrected and multivariate regression analysis, with male gender, old age, high creatinine, low ventilated lung volume, and high pneumonia extension [c-index (95% confidence interval)]. Enlarged MPAD (>31 mm) on CT has been reported as an independent predictor of mortality in COVID-19 (11).

The PA/AA ratio may be a predictor of poor prognosis. In our study, we had 320 in-patients whose mean PA/AA ratio was 0.78; 73 patients in the ICU whose PA/AA ratio was 1; and the mean PA/AA ratio of 51 patients who developed mortality was 1.03. Similarly, Yildiz et al. (12) examined the relationship between the severity of COVID-19 pneumonia and the diameter of the PA. A total of 101 patients with COVID-19 were included in this retrospective study. The patients were divided into three groups according to their CT images: 41 patients with mild pneumonia (group 1), 39 patients with moderate pneumonia (group 2), and 21 patients with severe pneumonia (group 3). In addition, the diameters of the MPAD, AA, and right and left PA diameters were calculated. Analyses show that increased MPAD is associated with poor prognosis in patients with COVID-19 pneumonia. In our study and a few other studies in the literature, PA diameter and the ratio of PA diameter to AA diameter are helpful for predicting clinical prognosis in patients with COVID-19.

The correlation between CT imaging parameters and clinical features in patients with patients has been investigated in recent studies. Eslami et al. (13) found that a PA/AA ratio >1 was

Table 5. Area under the curve for PA/AA and PA							
Variables	Area Sł	SH	р	95% CI			
				Highest	Lowest		
PA diameter	0.974	0.007	<0.001	0.960	0.988		
PA/AA ratio	0.997	0.002	<0.001	0.993	1.000		
AA: Ascending parts, DA: Pulmonary artery (1: Confidence interval							

Table 6. Optimal cut-off values for the PA diameter and PA/AA ratio Cut-off Sensitivity Youden's J index Positive likelihood ratio Negative likelihood ratio Specificity 0.9386 0.98 0.971 0.951 33.7931 0.020 PA/AA ratio 0.98 0.89 9.33 0.022 PA diameter (cm) 0.875 3.315

AA: Ascending aorta, PA: Pulmonary artery

Table 7. Prediction of in-hospital mortality in COVID-19 patients by logistic regression analysis					
	D	р	OR	95% CI OR	
	В			Lowest	Highest
CRP	0.004	0.396	1.004	0.995	1.013
D-dimer	0	0.670	1	1	1.001
LDH	0.003	0.202	1.003	0.998	1.009
Ferritin	0.001	0.412	1.001	0.999	1.002
PA/AA ration	5.402	< 0.001	221.890	17.918	2747.855
PA diameter	4.178	0.011	65.224	2.642	1609.932
Constant	-5.397	< 0.001	0.005		
AA: According ports DA: Du	Imanariu artariu CDDi Ciroactiu	a protain I DUI: La state dabi	udraganaca COVID 10: Caroni	uirus disaasa 2010. Cli Canfi	dance interval OB: Odds ratio

Ascending aorta, PA: Pulmonary artery, CRP: C-reactive protein, LDH: Lactate dehydrogenase, COVID-19: Coronavirus disease-2019, CI: Confidence interval, OR: Odds ratio

associated with extensive lung involvement and a nonsignificant increase in mortality (Odds ratio: 1.96 p=0.360) in 87 hospitalized COVID-19 patients. In addition, an increased cardiothoracic ratio is a strong predictor of mortality. According to Spagnolo et al. (14), previous chest CT scans of 45 COVID-19 patients showed that the PA/AA ratio increased after SARS-CoV-2 infection and was significantly correlated with the severity of pneumonia. In addition, enlargement of the PA diameter was associated with mortality in COVID-19 patients. Our study had a relatively more significant population than these two studies, with 255 patients. In our study, MPA was associated with in-hospital mortality according to the above cut-off values. MPA was an independent predictor of mortality as both a continuous and categorical variable in logistic regression analyzes In the logistic regression model, the PA/AA ratio and MPA diameter were independent predictors of mortality.

Pulmonary hypertension probably develops because of microvascular thrombi. Early diagnosis and aggressive anticoagulant treatment are crucial for these patients. Evaluating the PA/AA ratio with non-enhanced chest CT may predict the presence of underlying vascular thrombosis associated with poor prognosis. CT-measured indices may have predictive value for survival and extent of lung involvement in hospitalized COVID-19 patients and would be helpful for risk stratification of patients with COVID-19 and treatment decisions. In particular, increased PA diameter and PA/AA ratio are common in COVID-19 patients and can be strong predictors of mortality. Hayama et al. (15) examined the association between the PA/AA ratio and the clinical severity of COVID-19 infection. Twenty (19%) of 103 COVID-19 patients had severe respiratory exacerbations. Between the groups with and without severe respiratory exacerbation, the PA diameter (31.1±2.7 mm vs 25.4±3.5 mm, p<0.001) and the PA/AA ratio ( $0.97\pm0.11$  vs  $0.82\pm0.10$  p<0.001) were significantly different. This difference in PA/AA ratio was also significant in 74 patients under 65 (1.03±0.1 vs 0.84±0.09 p<0.001). The group with a PA/AA ratio >0.9 had a more severe respiratory exacerbation (p<0.001) than the group with a median PA/AA ratio cut-off point of ≤0.9. Kaplan-Meier survival curves for the PA/ AA ratio on admission showed an essential distinction between severe respiratory exacerbation and mortality during the hospital stay. Our study was conducted with a more significant population and found that mortality was significantly increased in patients with PA/AA >0.93.

## **Study Limitations**

This study has several limitations. First, this was a single-center, retrospective, and non-randomized study. We included patients with chest CT imaging and positive COVID-19 PCR test results in our study; therefore, these results cannot be generalized to

all COVID-19 patients. Our study does not include data from transthoracic echocardiography and right heart catheterization that would allow us to draw more precise conclusions about hemodynamic status and PA enlargement. We also had no data from previous CT scans, which hindered us from suggesting that PA enlargement occurred after SARS-CoV-2 infection.

## Conclusion

PA dilation and the ratio of PA diameter to AA diameter strongly predict in-hospital mortality in patients with hospitalized COVID-19. The PA diameter and PA/AA diameter ratio can be easily calculated from chest CT imaging and may help predict the prognosis of COVID-19 patients.

## Ethics

**Ethics Committee Approval:** The Ufuk University Hospital Ethics Committee and the Ministry of Health approved the study protocol (decision no: 22.05.12.05/07, date: 12.05.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

## **Authorship Contributions**

Surgical and Medical Practices: M.Ö., T.E., İ.Ç., Concept: M.Ö., T.E., İ.Ç., Design: M.Ö., T.E., Data Collection or Processing: M.Ö., Analysis or Interpretation: M.Ö., T.E., İ.Ç., Literature Search: M.Ö., T.E., İ.Ç., Writing: M.Ö., İ.Ç.

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Case Report

# Seizure and Altered Mental Status After Thoracentesis: Cerebral Air Embolism

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## Abstract

Cerebral air embolism (CAE) is a rare life-threatening condition. It may clinically mimic acute ischemic stroke by decreasing cerebral perfusion pressure and brain tissue oxygenation and may cause impaired consciousness and epileptic seizures. In its etiology; iatrogenic causes such as central venous catheterization, endoscopy, sclerotherapy, major surgeries, and invasive lung interventions are mostly seen. The most useful imaging method for diagnosis is cranial computed tomography (CT). In this presentation, we present the case of a 63-year-old male patient admitted to the emergency department (ED) with complaints of mental status changes and seizures and weakness in the left upper and lower extremities on physical examination. The patient had a history of thoracentesis performed three days ago and was discharged. Brain CT of the patient showed signs of newly developing CAE, and diffusion magnetic resonance imaging showed findings consistent with right middle cerebral artery infarction in his second admission. We thought that the symptoms of the patient, who had no history of additional intervention, were due to CAE, which developed as a complication of thoracentesis. Thoracentesis is one of the invasive procedures that can be applied for diagnostic/therapeutic purposes in the ED and does not have complications such as pneumothorax, hemothorax, soft tissue infection, or intra-abdominal organ injury. Physicians should be aware that CAE may also occur in patients who develop neurological deficits after thoracentesis. The clinician's high suspicion, prompt diagnosis, and treatment can be lifesaving.

Keywords: Cerebral air embolism, emergency department, thoracentesis

# Introduction

Thoracentesis is a frequent invasive procedure in emergency departments (EDs) for diagnosis and treatment. Although it is generally a non-hazardous procedure, it may cause life-threatening complications such as bleeding, pneumothorax, re-expansion pulmonary edema, spleen, or liver perforation. In addition to these complications, cerebral air embolism (CAE) is an extremely rare complication of thoracentesis (1,2). CAE is a rare life-threatening condition, and most are iatrogenic. In literature, it is defined that it may be related to antral venous catheterization, endoscopy, sclerotherapy, major surgeries, and invasive lung procedures (3,4). CAE may be 20% mortal in the acute period and may mimic acute ischemic stroke by decreasing cerebral perfusion pressure and brain tissue oxygenation. Because the symptoms and signs of air embolism are not specific, diagnosis may be difficult. Neurological symptoms may include

seizures, stroke, loss of consciousness, and altered mental status (5). The most useful imaging method in diagnosis is cranial computed tomography (CT), which shows intracranial air bubbles in 2/3 of the patients (6). Magnetic resonance imaging (MRI) also should be performed in patients with suspected infarcts with air embolism (3). The mechanism of CAE after thoracentesis is unclear. However, some hypotheses have been suggested. Air particles can pass through the arterial system in three different ways: directly through the venous to arterial system through pulmonary veins with a physiological shunt and cardiac septal defect (7,8). Arterial circulating air may obstruct microcirculation and cause ischemic endorgan damage. The most vulnerable organs affected by the microbubbles that cause arterial ischemia are the brain and heart. It is believed that 2 mL air in the cerebral arteries and 0.5 to 1 mL in the coronary circulation can be fatal (9,10). Because the brain consumes 15-20% of the cardiac volume, a large portion of the gas bubbles are transported to the brain by



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© Copyright 2023 The Emergency Physicians Association of Turkey / Eurasian Journal of Emergency Medicine published by Galenos Publishing House Licenced by Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) 4.0 International License. blood flow and cause the occlusion of cerebral vessels, such as in cerebral arterial gas embolism (11).

For the management of CAE in the EDs, vital functions should be supported and 100% oxygen therapy should be initiated. Positioning of the patient, a control of seizures, and intubation if necessary are other supportive treatment methods. The patient should be placed in the supine position. In the past, the trendelenburg position was used for treating CAE, but nowadays it is no longer recommended because it increases cerebral ischemia. Hyperbaric oxygen (HBO) treatment is recommended for definitive treatment. It increases the arterial partial pressure of oxygen, facilitates the dissolution of oxygen in plasma, and increases diffusion into the tissue. It can be used in patients with neurological deficits, end organ damage and hemodynamic deterioration (1,3,4).

# **Case Report**

A 63-year-old male presented to the ED with seizure and loss of consciousness. He had no history of additional disease. His blood pressure was 150/90 mmHg, pulse was 98 beats/min, respiratory rate was 22 breaths/min, and oxygen saturation was 92% (in the room air) as vital signs. Physical examination revealed disorientation with left upper and lower extremity weakness. His laboratory values were unremarkable. Three days ago, the patient underwent diagnostic thoracentesis for a newly diagnosed mass in the lung after presenting to the ED with dyspnea. Thoracentesis was not performed using an ultrasonography guide, and approximately 50 cc pleural fluid was removed. In his second admission, the patient was placed on 100% nonrebreather oxygen and CT scan with MRI was planned for intracranial hemorrhage or infarction. No signs of intracranial hemorrhage were detected on CT, but air bubbles on the right cerebral hemisphere confirmed the diagnosis of CAE (Figure 1). Brain diffusion-weighted MRI also showed hyperintense lesions in the right hemisphere compatible with the right middle cerebral artery (MCA) infarct (Figure 2). As the patient had no history of other intervention, we thought that air embolism had developed due to thoracentesis performed three days ago. After consultation with a neurologist, 0.6 mg intramuscular enoxaparin and 1,250 mg phenytoin intravenously in 250 mL saline over 45 min were given as medication. For etiological research, echocardiography was performed on the patient and it showed no patent foramen ovale (PFO) or atrial septal defect. Because the patient was unstable, he could not be transported for HBO treatment. He was admitted to the intensive care unit (ICU) for further examination and treatment. Diffusion MRI of the patient performed in the ICU also confirmed MCA infarction secondary to air embolism. The patient's ischemic cerebrovascular event and side findings were associated with air embolism. After being hospitalized and followed up for 45 days in the ICU, he was discharged with left hemiparesis sequelae and a peg tube inserted. Antiepilectic and anticoagulant treatments were prescribed.

## Discussion

Our patient had no etiologic factors that could cause CAE, such as trauma, surgical intervention, catheterization, and PFO. We therefore thought that CAE may be due to thoracentesis. He had an air embolism in the right hemisphere on CT imaging and infarct findings in the same area detected on MR imaging. We thought that the infarct area developed secondary to ischemia caused by air embolism.

In a study evaluating 15 patients with CAE; it was observed that 80% of the patients presented with focal deficit and/or coma (53%). Seizures were detected in 47% of the patients (12). Although there are studies proving that brain CT scans show CAE in 2/3 of the patients (6), the brain CT scans performed in this study were sensitive in only 4 of 13 patients, whereas MRI scans were found to show multifocal diffusion restriction (12). In the patient we presented, air embolism was detected in the brain CT performed in the acute period, and diffusion limitations in MRI. In studies in the literature, imaging findings such as intracranial air embolisms and ischemic or edematous lesions were associated with increased mortality but were not statistically significant (6). Heckmann et al. (9) showed that the presence of focal neurological signs, encephalopathy, or epileptic seizures were not individual markers of mortality. Similarly, CAE detected in our case who presented with the complaints



**Figure 1.** Arrows show cerebral air embolism on the right cerebral hemisphere in computed tomography imaging



Figure 2. Arrows show acute cerebral infarct on the right cerebral hemisphere in magnetic resonance imaging

of altered consciousness, seizure, and left hemiparesis did not cause mortality but caused morbidity.

## Conclusion

CAE is a rare but life-threatening condition. When a neurological event (altered mental status, seizure, focal neurologic signs) develops after venous catheterization, neurosurgical, vascular, and cardiac surgeries, gastroenterology procedures, pulmonary barotrauma, and invasive lung procedures, it should always be suspected. Rapid diagnosis and supportive treatment with HBO therapy can be lifesaving.

## Ethics

**Informed Consent:** Informed consent was not required as no personally identifying information was used this case.

Peer-review: Externally peer-reviewed.

### **Authorship Contributions**

Surgical and Medical Practices: Ç.S.B., Concept: Ç.S.B., Design: H.N., Data Collection or Processing: H.N., Analysis or Interpretation: H.N., Literature Search: C.A., Writing: C.A.

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# **Epiglottitis with a Complication of Epiglottic Abscess:** A Case Report and Review of the Literature

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## Abstract

Epiglottitis is a life-threatening condition that can result in a 10% mortality rate in adults. This case report presents the case of a 34-year-old man with epiglottitis complicated by an epiglottic abscess (EA). The patient was successfully treated with incision and drainage under general anesthesia. EA is a rare complication of epiglottitis, and prompt diagnosis and management are crucial for preventing airway compromise and respiratory failure. This report reviews the literature on epiglottitis and EAs, including their presentation, diagnosis, and management.

Keywords: Epiglottitis, epiglottic abscess, airway obstruction, respiratory failure

# Introduction

Epiglottitis is a potentially life-threatening condition characterized by inflammation of the epiglottis, which can lead to a mortality rate of 10% in adults (1). This condition can progress to airway obstruction and respiratory failure (1). Patients with epiglottitis typically present with sudden onset of severe sore throat, dysphagia, stridor, retractions, and cyanosis (2). Prompt diagnosis and management are essential for preventing airway compromise and respiratory failure (2). We report a case of a 34-year-old man with a complaint of dysphagia and severe pharyngodynia who, after close examination and workup, was found to have epiglottitis with an epiglottic abscess (EA). We discuss the diagnostic approach to such cases and prompt management of critical condition to avoid possible complications.

# **Case Report**

A 34-year-old previously healthy male presented to the emergency department with a 2-day history of dysphagia and severe pharyngodynia. Prior to his presentation, the patient had received antibiotics and antipyretics at a private healthcare facility; however, no significant improvement in his symptoms was observed. The patient experienced difficulty tolerating oral intake and reported hoarseness and a "hot potato" voice. He had

no known drug allergies and a non-significant medical history. The patient denied any history of alcohol or tobacco use. Upon reviewing his body systems, he reported fever and chills but denied visual disturbances, headaches, vomiting, or nausea, and had no other complaints.

Upon examination, the patient appeared unwell and dehydrated. Anterior neck examination revealed tenderness, particularly on the right side. Throat examination using a tongue depressor revealed no significant inflammation or erythema. The patient could move his neck without signs of meningism. Ear, nose, and throat examinations were unremarkable. The differential diagnosis included retropharyngeal abscess, pharyngitis, and epiglottitis.

Laboratory testing revealed a white blood cell count of 22.07x10<sup>9</sup>/L, a neutrophil count of 18.45x10<sup>9</sup>/L, and an elevated C-reactive protein level of 174 mg/L. Urea and electrolyte levels were within normal limits. A lateral soft tissue neck X-ray (Figure 1) displayed a thumbprint sign, indicative of swollen epiglottis. The case was discussed with the on-call ear, nose, and throat physician, who advised obtaining a computed tomography (CT) scan with contrast to rule out an abscess. The neck CT scan with contrast (Figure 2) revealed diffusely swollen epiglottis with peripheral enhancing hypodensity measuring 3 cm 2.8 cm, consistent with an EA.



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The patient was taken to the operating theater as a level 1 patient, where he was intubated by an anesthetist using fiberoptic intubation. Incision and drainage of the EA were performed under direct laryngoscopy (Figure 3). Postoperatively, the patient was admitted to the surgical intensive care unit for 72 h while intubated. He received intravenous (IV) dexamethasone, cefepime, and metronidazole. Extubation was performed when the inflammatory markers showed marked improvement, and repeated CT demonstrated complete resolution of the previously observed EA (Figure 4). Tissue culture results revealed *K*. *pneumoniae* and *Escherichia coli*.



**Figure 1.** Lateral neck X-ray demonstrating the thumbprint sign, indicative of swollen epiglottis



**Figure 2.** Contrast-enhanced computed tomography scan revealing epiglottitis accompanied by an epiglottic abscess

# Discussion

EA, with an incidence of 4%, is generally considered an uncommon complication of acute epiglottitis (also referred to as supraglottitis). EA predominantly affects males, and compared withchildren, adults are more likely to experience neck discomfort and voice changes as additional symptoms (3). Voice alterations are more commonly reported by patients with EA (4), whereas sore throat is the most prevalent symptom in other studies, followed by dysphagia, voice change, and dyspnea (5,6).

Pre-existing diabetes mellitus is a potential risk factor for the development of acute epiglottitis and EA, particularly in males aged 35 to 64 years. A history of foreign body ingestion is another risk factor for EA (7), as is incomplete vaccination, particularly for H. influenzae type B.

The diagnosis of epiglottitis relies on the physician's suspicion along with the patient's acute clinical presentation. If there are signs of airway compromise, a lateral neck X-ray may confirm the condition through the "thumb sign" but is not always necessary. In cases where initial imaging is inconclusive, flexible fiberoptic laryngoscopy in the operating room may be considered. When an EA is suspected, a CT scan is an appropriate diagnostic test for stable patients (8).

The primary management step for epiglottitis is airway protection (9). Delayed or inadequate treatment may lead to life-threatening airway obstruction (9). Patients who present with clinical features of airway obstruction or have been diagnosed with EA should be transported to the operating room for further airway management and drainage, often following tracheal intubation (9). Antibiotic overuse, potentially leading to the development and spread of antimicrobial resistance, may contribute to the occurrence of EA. Epiglottitis with EA is more complex and challenging to treat than pure epiglottitis.

Various treatments have been described in the literature, including incision and drainage under general anesthesia (10,11), spinal needle aspiration (12,13), and other therapies that serve as alternatives or adjuncts to antibiotic therapy (10-13). However, no consensus has been reached regarding the optimal treatment approach for EA.

A recent study reported that individuals with EA who were treated with antibiotics and indirect laryngeal biopsy forceps experienced shorter hospital stays and faster symptom relief than those who received medication alone. The use of laryngeal biopsy forceps under local anesthesia instead of general anesthesia for treating EA was found to be more practical, simpler, and inexpensive (13).



Figure 3. Intraoperative findings using a laryngoscope, displaying epiglottitis with an epiglottic abscess. A) Pre-intubation. B) Pre-incision and drainage. C) Post-incision and drainage



**Figure 4.** Contrast-enhanced computed tomography scan presenting near-complete resolution of the epiglottic abscess (sagittal view)

# Conclusion

In conclusion, this case report underscores the importance of maintaining a high index of suspicion for EA as a potential complication of epiglottitis, particularly in adult males. Prompt diagnosis and management, including securing the airway, administering IV antibiotics, and performing surgical drainage, are crucial in preventing life-threatening complications and ensuring a favorable outcome for the patient. Clinicians should be vigilant for symptoms such as severe sore throat, dysphagia, odynophagia, fever, and rapid progression of symptoms in the context of known or suspected epiglottitis. Collaboration among emergency physicians, intensivists, and otolaryngologists is essential to provide timely and effective care to these patients. Further research is needed to better understand the risk factors, optimal management strategies, and long-term outcomes of patients with EAs.

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## Ethics

**Informed Consent:** The patient provided informed consent for the publication of this case report and the accompanying images (verbal consent).

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## **Authorship Contributions**

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search -Writing: A.D., A.A., H.A., M.H., I.A.

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Case Report

Eurasian J Emerg Med. 2023;22(4): 255-7

# Hypothermia as a Medication Side Effect

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### Abstract

In humans, the body temperature stabilizes in the range of 36.5-37.3 °C; below 35 °C is defined as hypothermia. The use of olanzapine, an antipsychotic drug, is one of the least reported drugs in the etiology of hypothermia. A 67-year-old female patient was admitted to the emergency department. Her body temperature was measured 27.8 °C. No cold exposure was found on the first evaluation by the ambulance crew. It was learned that she used olanzapine 10 mg and had taken her first dose 8 h ago. The patient's hypothermia was evaluated because of olanzapine use. Body temperature regulation disorders due to antipsychotic drug use are mostly defined as hyperthermia. It has been reported that antipsychotic drugs may very rarely play a role in the etiology of hypothermia and hyperthermia. Olanzapine is used for treating psychotic diseases by acting via an antagonist mechanism on 5-HT2A/C and dopamine D2 receptors located in the hypothalamic region. The hypothalamus is thought to play a crucial role in central thermoregulation and providing the therapeutic efficacy of antipsychotic drugs. Antipsychotics may also cause hypothermia by blocking peripheral b2 receptors. These common mechanisms explain the cause of hypothermia in this study due to olanzapine use. Olanzapine use should be considered in cases of unexplained hypothermia in the emergency department. Routine body temperature monitoring should be considered in patients who are administered antipsychotic drugs with hypothermia in the side-effect profile, such as olanzapine.

Keywords: Hypothermia, side effect, antipsychotic drug, olanzapine

# Introduction

In humans, the body temperature stabilizes in the range of 36.5-37.3 °C, below 35 °C is defined as hypothermia (1). Hypothermia is categorized into three classes: mild (35-33 °C), moderate (33-28 °C) and deep (<28 °C) (1). Depending on the degree of hypothermia, chills and tremors, unconsciousness, deep coma, and even cardiac arrest (CA) may occur (2). Hypothermia may occur as a result of insufficient protection against cold exposure, hypoglycemia, adrenal insufficiency, hypothyroidism, therapeutic applications, and drugs (1). Hypothermia due to antipsychotic drugs has been reported very rarely (3).

Body temperature regulation disorders due to antipsychotic drug use are mostly defined as hyperthermia (4). In this case report, we present a case of hypothermia due to olanzapine use in light of the literature.

# **Case Report**

A 67-year-old female patient was brought to the emergency department by ambulance crews on a day when the air temperature was 17 degrees Celsius, with complaints of immobility in her 4 extremities and impaired speech. No history could be taken from the patient because of speech disorder. She had no history of any other disease, such as diabetes mellitus (DM), hypothyroidism, adrenal insufficiency, cerebrovascular disease (CVD), or ischemic heart disease, apart from known schizophrenia. It was learned that she used olanzapine 10 mg and had taken her first dose 8 h ago. In the emergency department, the body temperature was measured on the skin with a bedside monitor, and it was found to be 27.8 °C (82.04°F), heart rate 33 beats/minute, blood pressure 80/50 mmHg, respiratory rate 14/minute, and oxygen saturation 94% in room air. Deep hypothermia was detected in the patient. No cold exposure was found on the first evaluation by the ambulance



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© Copyright 2023 The Emergency Physicians Association of Turkey / Eurasian Journal of Emergency Medicine published by Galenos Publishing House. Licenced by Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) 4.0 International License. crew. On physical examination, the patient was confused, her eyes were open spontaneously, she had no verbal response, and she avoided stimuli. The skin and mucous membranes were dry, there was no jugular fullness, and other systemic examinations were within normal limits. In addition, an increase in RR and QT wave intervals, first-degree atrioventricular block, and sinus bradycardia were observed in the first electrocardiogram (ECG) in the emergency department (Figure 1).

In terms of the etiology of hypothermia and impaired consciousness, serum glucose 125 mg/dL, sodium 136 mEq/L, urea 45, creatinine, glomerular filtration rate, cortisol level, thyroid stimulating hormone, free triiodiothyronine, free thyroxine, and complete blood count were within normal limits.

Posteroanterior chest X-ray and brain computed tomography were within normal limits, and no ischemic changes were observed on diffusion magnetic resonance imaging. The patient's hypothermia was evaluated because of olanzapine use.

For the treatment of hypothermia, 1000 mL of intravenous bolus hydration with warmed 0.9% sodium chloride was applied to the patient, and the patient was covered with a thermal blanket. In the first hour of her treatment, her blood pressure was 110/60 mmHg, heart rate was 60 beats/min, and body temperature was 29.7 °C.

The patient, who was admitted to the intensive care unit, continued to be warmed with heated intravenous fluid applications and external active air heater systems. Body temperature was monitored in terms of hypothermia on the skin and recorded hourly (Figure 2).







Figure 2. First electrocardiogram in the emergency department

In the body temperature follow-ups, the body temperature reached 36.5 °C at the 6<sup>th</sup> hour of treatment. In the control evaluation performed at the 24<sup>th</sup> hour of the patient, it was found that she was conscious, oriented, cooperative, and had full muscle strength in 4 extremities, and motor and sensory examinations were normal. The patient's olanzapine use was terminated, and she was referred to the psychiatric clinic for drug regulation.

## Discussion

Body temperature is the basic vital parameter in the evaluation of many diseases and critical patients that require emergency treatment in the emergency department and is measured from the pulmonary artery as the gold standard (5). Besides the pulmonary artery, due to both their invasiveness and the length of the application period, measurements made through the esophagus, bladder, and rectum have left their place to measurements made from the temporal artery, tympanic, or forehead with infrared methods that can be applied more easily in emergency services (5).

In the treatment process of hypothermia, the infusion of heated fluids, delivery of heated fluids to the body cavities, and heated air can be used, while the body temperature of the patients can be monitored with systems that can make hypothermic measurements (6).

In our case, heated fluid infusion and heated air were used for treating hypothermia, and a skin sensor placed on the back of the patient, posterior to the pulmonary region, was used in the follow-up.

Dopamine D1 and D2, alpha-1, 5-hydroxytryptamine 1 and 2 receptors located in the hypothalamus are thought to play a crucial role in central thermoregulation as well as providing the therapeutic efficacy of antipsychotic drugs (7). Antipsychotics may also cause hypothermia by blocking peripheral b2 receptors (8). These common mechanisms explain the etiology of hypothermia in our case due to olanzapine use.

The hypothermic effects of antipsychotic drugs have been tested with animal experiments, and it has been shown that therapeutic hypothermia can be created by administering olanzapine at a daily treatment dose (9). This supports the role of olanzapine in the etiology of hypothermia in our case.

Hypothermia may cause changes in ECG by affecting cardiac electrophysiology (1). Deep hypothermia may cause an increase in the RR interval in wavelengths, an increase in the P wave amplitude, an increase in the PR interval, first- to third-degree atrioventricular blocks, an increase in the QRS width and an increase in the QT interval, and atrial fibrillation, ventricular fibrillation (VF), and asystole may also be seen as arrhythmia (2). An increase in the RR and QT wave intervals, first-degree atrioventricular block, and sinus bradycardia were associated with hypothermia in the ECG of our case.

When CA develops in a hypothermic patient, while chest compression and ventilation are performed in the same way as a normothermic patient in cardiopulmonary resuscitation (CPR) practices, there are differences in electrical therapy and drug applications in the case of VF (2,10). When VF develops, no shock is applied again until the body temperature rises above 30 °C after three shocks (2). Epinephrine is not recommended to be administered below 30 °C, and when it rises above 30 °C, it is recommended to double the application time interval and apply it every 6-10 minutes (2). Delayed CPR can be applied in CA below 28 °C, and it is recommended to return to normal CPR protocols above 35 °C (2).

In the literature, such predisposing factors as infection, hypothyroidism, DM, and long-term drug use are observed in patients who develop hypothermia (11). The absence of predisposing factors in our case supports the association of olanzapine with the etiology of hypothermia.

Body temperature measurement and monitoring are not routinely performed in patients using antipsychotic medication (12). Therefore, it is unknown how often hypothermia occurs in the side-effect profile (12). Considering the timing of the reported cases of hypothermia, it was reported that 20% of them occurred during the long period of drug use, mostly in the first 7-10 days (8). In our case, hypothermia also occurred on the first day of drug use. It can be concluded that body temperature monitoring in the first 10-day period will be beneficial in patients who started to use antipsychotics, especially olanzapine.

# Conclusion

In conclusion, olanzapine use should be considered in cases of unexplained hypothermia in the emergency department. Routine body temperature monitoring should be considered in patients who are administered antipsychotic drugs with hypothermia in the side-effect profile, such as olanzapine.

## Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

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# **Bilateral Lingual Artery Embolization to Control Massive Oral Bleeding That Leads to Cardiac Arrest**

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# Abstract

Oral cavity structures receive abundant perfusion from the branches of the external carotid artery. Although hemorrhage is a common complication of oral cancer, bleeding from a cancerous mouth can be a devastating event in the emergency department. Lingual artery embolization is a minimally invasive interventional radiology procedure that has rarely been reported in the literature. This case involves a patient with tongue cancer who experienced massive oral bleeding leading to cardiac arrest. Fortunately, the patient was successfully resuscitated, and spontaneous circulation was restored. Diagnostic angiography confirmed the presence of pseudoaneurysm in the lingual artery. Ultimately, bleeding was definitively controlled through bilateral lingual artery embolization. This case underscores the critical importance of a multidisciplinary approach involving emergency physicians, otolaryngologists, and interventional radiologists in managing complex vascular lesions in the head and neck. Furthermore, it contributes to the growing body of evidence supporting the use of embolization techniques as a valuable tool in the management of vascular lesions in the head and neck region.

Keywords: Lingual artery embolization, oral bleeding, tongue cancer

# Introduction

One of the principal branches of the external carotid artery is the lingual artery, which is responsible for supplying blood to the tongue and oral cavity. The lingual artery causes several branches that nourish various structures in the lingual and sublingual regions. These branches extend their supply to the jaw, buccal and gingival mucosa, different parts of the tongue (including the body, tip, and posterior region), palatoglossal arch, soft palate, lingual tonsil, epiglottis, and mylohyoid muscle (1).

Tongue cancer is the most prevalent malignant tumor in oral cancer cases. Advanced tongue cancer or radiotherapy often leads to a common complication: hemorrhage. Bleeding can be profuse, and without prompt and effective treatment, it may lead to suffocation, shock, and high mortality rates (2).

This case revolves around a patient with tongue cancer who experienced massive oral bleeding, which ultimately resulted in cardiac arrest. Fortunately, the patient was successfully resuscitated, and spontaneous circulation was restored. Subsequently, the bleeding was definitively controlled through bilateral lingual artery embolization.

# **Case Report**

A 42-year-old male, a known case of locally invasive squamous cell carcinoma (SCC) of the tongue and left buccal mucosa cancer, presented to the emergency department with bleeding from the tumor bed and intermittent low-grade fever for the past day. The bleeding had been increasing and was associated with blood clots. The patient also reported facial pain and swelling. His vital signs showed a blood pressure of 109/65 mmHg, a pulse rate of 88 beats/min, a temperature of 37.2 °C, a respiratory rate of 15 breaths/min, and an oxygen saturation of 97% on room air.

The patient had previously received chemotherapyand multiple cycles of radiotherapy and was now on immunotherapy. He underwent tracheostomy and a percutaneous endoscopic gastrostomy tube for feeding. Notably, the patient was not on any antiplatelet or anticoagulant medications.



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Physical examination revealed left jaw tenderness, swelling, and limited mouth opening due to pre-existing trismus, whereas the rest of the examination was unremarkable. The bleeding was initially suctioned and packed with adrenaline-soaked swabs, which successfully controlled the bleeding. The patient was scheduled for admission to the oncology department because of possible sepsis. However, the bleeding recurred, necessitating additional packing with tranexamic acid-soaked materials and the initiation of intravenous tranexamic acid, which successfully halted the bleeding.

Laboratory tests indicated a prothrombin time of 13.4 s (normal range: 9.5-12.5), an international normalised ratio of 1.21 (normal range: 0.87-1.15), an activated partial thromboplastin time of 27.9 s (normal range: 22.2-34.2), and a fibrinogen level of 6.30 g/L (normal range: 1.5-3.87). Blood tests showed a white blood cell count of  $30.3 \times 10^9$ /L (normal range: 4.5-11), hemoglobin level of 8.2 g/L (normal range: 13.2-17.3), and platelet count of  $389 \times 10^9$ /L (normal range: 140-400). His baseline hemoglobin level ranged from 8.9 to 9.5 g/L.

The case was discussed with an otolaryngologist, and the decision was made to arrange arterial embolization through interventional radiology because of the patient's history of multiple presentations with oral bleeding. The interventional radiologist expressed concerns regarding the risk of stroke with bilateral lingual artery embolization. However, the patient experienced massive bleeding following a significant episode of vomiting blood from his mouth and tracheostomy tube. His vital signs deteriorated rapidly, with a blood pressure drop to 70/35 mmHg, a pulse rate of 125 beats/min, and an oxygen saturation decrease to 70% in room air.

Efforts to control the bleeding, including suction and multiple attempts at packing, were unsuccessful, leading to cardiac arrest. Resuscitation efforts were initiated, reversible causes of cardiac arrest were ruled out, and hypovolemic shock was identified as the primary cause. Consequently, a massive transfusion protocol was activated, and the patient received packed red blood cells, fresh frozen plasma, cryoprecipitate, platelets, and recombinant activated factor VII (Novo 7). Multiple doses of epinephrine, sodium bicarbonate, and dextrose were also administered. Fortunately, the patient achieved a return of spontaneous circulation after 20 min, and the bleeding was temporarily controlled.

The otolaryngologist replaced the tracheostomy tube, and the patient was then transferred to interventional radiology for embolization after stabilization. A bilateral internal and external carotid artery angiogram was performed (Figure 1), revealing evidence of abnormal tumor vascularity supplied by the lingual artery, with a new false aneurysm affecting the left lingual artery measuring 3x5 mm in diameter.

Bilateral lingual artery embolization was performed using metallic coils and 500-700 particles through the Progreat Microcatheter until stasis was achieved, without complications (Figure 2). The bleeding was successfully controlled, and the



**Figure 1.** A bilateral internal and external carotid artery angiogram indicated the presence of abnormal tumor vascularity supplied by the lingual artery. Additionally, it revealed a newly formed false aneurysm in the left lingual artery, measuring 3x5 mm in diameter



**Figure 2.** A bilateral internal and external carotid artery angiogram confirmed the successful embolization of the bilateral lingual artery using metallic coils and 500-700 particles delivered through the Progreat Microcatheter

patient's blood pressure improved to 105/67. The patient was then transferred to the intensive care unit, where he remained for several days before being transferred to the medical floor. The patient had an uneventful admission and was subsequently discharged to a homecare facility.

# Discussion

Patients with oral SCC often experience bleeding, which can manifest as sudden catastrophic events, occasional massive bleeding, or persistent low-volume leakage. Hemorrhage in oral SCC is associated with local tumor irradiation, spontaneous tumor bleeding, and chemotherapy. In cases of recurrent illness, bleeding due to chemotherapy-induced thrombocytopenia, a consequence of prior chemoradiotherapy (CRT), can also be significant. Free radicals from CRT may damage the adventitial vasa vasorum, leading to early atherosclerosis, adventitial fibrosis, wall thinning in the carotid artery, and even thrombosis. Furthermore, high total and fractional doses of radiation therapy, especially in cases of repeated irradiation, may increase the risk of vascular mucosal damage (3).

Notably, surgery has also been linked to bleeding in oral SCC patients, in addition to CRT. Some patients have reported developing pseudoneurysms up to 20 years after extensive neck dissection and radiotherapy. Bacterial infections at the surgical sites of head and neck surgeries have been associated with vasa vasorum thrombosis and artery wall damage (3).

The lingual artery, typically extending from the dorsal end of the tongue to its tip, covers approximately 75% of the tongue's length. For approximately three-quarters of its length, the artery follows a lateral and inferior course (1).

The robust blood supply in the oral cavity is attributed to the presence of collateral vessels. Lingual artery embolization is a specialized interventional radiological procedure that plays a significant role in the comprehensive management of tongue cancer. In cases where advanced cancers affect local vascular systems, lingual artery embolization serves as a crucial adjuvant therapy to address both the oncological and symptomatic aspects of the disease. When significant bleeding cannot be controlled by mechanical pressure and packing, embolization or ligation is recommended (4).

Given the complex anatomy of the head and neck and the abundant blood supply, surgical treatment can be challenging. However, super-selective lingual artery embolization is a straightforward approachthat effectively stops bleeding and allows for rapid identification of blood vessels (2). Lingual artery embolization in the context of tongue cancer serves several essential purposes:

**1. Hemostasis:** The primary goal is to achieve hemostasis and prevent further bleeding episodes. Tumor-induced vascular damage can weaken the lingual artery, making it prone to rupture. Embolization effectively occludes the feeding vessels, thereby controlling hemorrhage and stabilizing the patient's condition (2).

**2. Symptom Relief:** In addition to its hemostatic benefits, lingual artery embolization can significantly alleviate the symptoms associated with tumor-related bleeding. This includes dysphagia, odynophagia, and speech difficulties, which can profoundly impact a patient's quality of life (2).

**3. Facilitation of Surgery or Radiation Therapy:** In some cases, embolization may be performed as a preoperative or pre-radiation therapy measure. By reducing tumor vascularity and minimizing the risk of intraoperative bleeding, it enhances the safety and feasibility of surgical resection or radiation therapy (5).

To address significant bleeding by blocking the entire channel, the lingual artery is often ligated above the hyoid bone. After ligating the lingual artery stem at its origin from the external carotidartery, healthy collateral circulation may remain (4).

This case report contributes to the growing body of evidence supporting the use of embolization techniques in the management of vascular lesions in the head and neck region. Moreover, it underscores the importance of prompt recognition and intervention in cases of lingual artery pseudoaneurysms, which can have life-threatening consequences if left untreated.

# Conclusion

Bleeding associated with mouth cancer can be a devastating emergency event, potentially leading to cardiac arrest. It is imperative to initiate early and appropriate management, fostering teamwork among various specialties. Interventional radiology can play a crucial role in precisely identifying the responsible blood vessels, and lingual artery embolization has emerged as a swift and effective method for controlling bleeding with minimal complications.

## Ethics

**Informed Consent:** Consent to the case's publication and the pictures taken from the patient.

**Peer-review:** Externally peer-reviewed.

## **Authorship Contributions**

Surgical and Medical Practices: M.M.E., T.J., Concept: T.J., Design: M.M.E., Data Collection or Processing: M.M.E., Analysis or Interpretation: M.M.E., Literature Search: M.M.E., Writing: M.M.E.

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