EPAT
Emergency Physicians Association of Turkey

EAJEM

Eurasian Journal of Emergency Medicine

Citation abbreviation: Eurasian J Emerg Med

ISSN 2149-5807 • EISSN 2149-6048

Volume: 21
Issue: 2

www.eajem.com

June
2022

galenos yayınevi

Official Journal of Emergency Physicians Association of Turkey

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Turkey **Phone:** +90 (212) 621 99 25 **Fax:** +90 (212) 621 99 27
E-mail: info@galenos.com.tr/yayin@galenos.com.tr **Web:** www.galenos.com.tr **Publisher Certificate Number:** 14521
Printing at: Son Sürat Daktilo Dijital Baskı San. Tic. Ltd. Şti.
Gayrettepe Mah. Yıldızposta Cad. Evren Sitesi A Blok No: 32 D: 1-3 34349 Beşiktaş, İstanbul, Turkey
Phone: +90 (212) 288 45 75
Printing Date: June 2022 **ISSN:** 2149-5807 **E-ISSN:** 2149-6048
International scientific journal published quarterly.

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

Past editors

Erden Erol Ünlüer
Department of Emergency Medicine, Uşak University School of Medicine, Uşak, Turkey
erolerdenun@yahoo.com
ORCID ID: 0000-0003-0334-7440
İsa Kılıçaslan
Department of Emergency Medicine, Gazi University School of Medicine, Ankara, Turkey
isakilicaslan@hotmail.com
ORCID ID: orcid.org/0000-0002-0330-2595

List of the reviewers who reviewed papers for Eurasian Journal of Emergency Medicine June 2022.

Abdülkadir Gündüz
Abuzer Coşkun
Ahmet Baydın
Ahmet Demircan
Ali Bıdarı
Ali Karakuş
Arif Karagöz
Ataman Köse
Ayhan Aköz
Ayhan Sarıtaş
Badria Al Hatali
Bedia Gulen
Erdal Demirtaş
Erdinç Acar
Ferhat İçme
Feride Sinem Akgün
Gülşah Çikrikçi Işik
Iş Sarıtaş
Mehmet Oğuzhan Ay
Muhammet Gokhan Turtay
Mustafa Boğan
Mustafa Sabak
Nazire Belgin Akıllı
Oğuzhan Bol
Özgür Söğüt
Samad Shams Vahdati
Sertaç Güler
Tufan Alatlı
Zamir Kemal Ertürk

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

AIMS AND SCOPE

Eurasian Journal of Emergency Medicine (Eurasian J Emerg Med) is the open access, scientific publication organ of the Emergency Medicine 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).

Eurasian Journal of Emergency Medicine is indexed in Web of Science-Emerging Sources Citation Index, TUBITAK ULAKBIM TR Index, EBSCO, Directory of Research Journals Indexing, J-Gate, Türk Medline, Türkiye Atıf Dizini, ProQuest, CABI, British Library and Index Copernicus.

Processing and publication are free of charge with Eurasian Journal of Emergency Medicine. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system which is available through the journal's web page at www.eajem.com. Journal's guidelines, technical information and the required forms are available on the journal's web page.

All expenses of the journal are covered by the Emergency Medicine Physicians' Association of Turkey. Pharmaceutical advertisements may be published in the printed copies of the journal. Potential advertisers should get in contact with the Editorial Office. Advertisement images are only published upon Editor in Chief's approval.

Statements or opinions expressed in the manuscripts published in the journal reflect the views of the author(s) and not the opinions of the Eurasian Journal of Emergency Medicine, the editors, the editorial board and/or the publisher, GALENOS; the editors, the editorial board and the publisher disclaim any responsibility or liability for such materials.

Editorial Office

Prof. Salvatore Di Somma, MD PhD

Emergency Medicine

Department of Medical-Surgery Sciences and Translational Mediicne

Chairman Postgraduate School of Emergency Medicine

Faculty of Medicine and Psychology

University of Rome Sapienza

Rome, Italy

E-mail: salvatore.disomma@uniroma1.it

Phone: +39348.3316131

Open Access Policy

This journal provides immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge.

Open Access Policy is based on the rules of the Budapest Open Access Initiative (BOAI) http://www.budapestopenaccessinitiative.org/. By "open access" to peer-reviewed research literature, we mean its free availability on the public internet, permitting any users to read, download, copy, distribute, print, search, or link to the full texts of these articles, crawl them for indexing, pass them as data to software, or use them for any other lawful purpose, without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. The only constraint on reproduction and distribution, and the only role for copyright in this domain, should be to give authors control over the integrity of their work and the right to be properly acknowledged and cited.

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

INSTRUCTIONS TO AUTHORS

Eurasian Journal of Emergency Medicine (Eurasian J Emerg Med), as a double-blind peer reviewed journal published by the Emergency Medicine Physicians' Association of Turkey, publishes original articles on clinical, experimental and basic sciences in the Emergency Medicine field, review articles covering basic and up-to-date subjects, case reports, short editorial manuscripts and manuscripts covering medicine history and publication and research ethics.

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.

Manuscripts submitted to Eurasian Journal of Emergency Medicine will go through a double blind peer review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in the field in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation processes of manuscripts submitted by editors or the editorial board members of the journal. The Editor in Chief is the final authority in the decision making process of all submissions.

An approval of research protocols by Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", amended in October 2013, www.wma.net) is required for experimental, clinical and drug studies and some case reports. If required, ethics committee reports or an equivalent official document may be requested from the authors. For manuscripts concerning experimental research on humans, a statement should be included that shows informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information on patient consent, name of the ethics committee and the ethics committee approval number should also be stated in the materials and methods section of the manuscript. It is the authors' responsibility to carefully protect the patients' anonymity. For photographs that may reveal the identity of the patients, releases signed by the patient or their legal representative should be enclosed.

All submissions are screened by a similarity detection software (iThenticate by CrossCheck).

In the event of an alleged or suspected research misconduct, including plagiarism, citation manipulation, and data falsification/fabrication, among others, the Editorial Board will follow and act in accordance with COPE guidelines.

Each individual listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship be based on the following 4 criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

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

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

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for the parts of the work he or she has done, an author should be able to identify which co-authors are responsible for specific other parts of the work. In addition, authors should have confidence in the integrity of the contributions of their coauthors.

All those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria should be acknowledged in the title page of the manuscript.

Eurasian Journal of Emergency Medicine requires corresponding authors to submit a signed and scanned version of the authorship contribution form (available for download through www.eajem.com) during the initial submission process in order to act appropriately to authorship rights and prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship", the submission will be rejected without further review. As part of submission of the manuscript, the corresponding author should also send a short statement declaring that he/she accepts to undertake all the responsibility for authorship during the submission and review stages of the manuscript.

Eurasian Journal of Emergency Medicine requires and encourages the authors and the individuals involved in the evaluation process of submitted manuscripts to disclose any existing or potential conflicts of interests including financial, consultant, institutional and other relationships that might lead to bias or a conflict of interest.

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

INSTRUCTIONS TO AUTHORS

Any financial grants or other support received for a submitted study from individuals or institutions should be disclosed to the Editorial Board and to disclose potential conflicts of interest ICMJE Potential Conflict of Interest Disclosure Form should be filled in and submitted by all contributing authors. Cases of potential conflicts of interest of editors, authors and reviewers are resolved by the journal's Editorial Board within the scope of COPE and ICMJE guidelines.

Editorial Board of the journal handles appeal and complaint cases within the scope of COPE guidelines. Authors should get in direct contact with the editorial office regarding their appeals and complaints.

When needed, an ombudsperson can be assigned to resolve cases that cannot be resolved internally. The Editor in Chief is the final authority in the decision making process of appeals and complaints. When submitting a manuscript to the Eurasian Journal of Emergency Medicine, authors accept to assign the copyright of their manuscript to Emergency Medicine Physicians' Association of Turkey. If rejected for publication, the copyright of the manuscript will be assigned back to the authors. Eurasian Journal of Emergency Medicine requires each submission to be accompanied by a Copyright Transfer Form (available for download at www.eajem.com). When using previously published content, including figures, tables, or any other material in both print and electronic formats, authors must obtain permission from the copyright holder.

Statements or opinions expressed in the manuscripts published in Eurasian Journal of Emergency Medicine reflect the views of the author(s) and not the opinions of the editors, the editorial board or the publisher; the editors, the editorial board and the publisher disclaim any responsibility or liability for such materials. The final responsibility in regard to the published content rests with the authors.

Manuscript Preparation

The manuscripts should be prepared in accordance with ICMJE-Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (updated in December 2017 -http://www.icmje. org/icmje-recommendations.pdf). Authors are required to prepare manuscripts in accordance with CONSORT guidelines for randomized research studies, STROBE guidelines for observational original research studies, STARD guidelines for studies on diagnostic accuracy, PRISMA guidelines for systematic reviews and meta-analysis, ARRIVE guidelines for experimental animal studies and TREND guidelines for non-randomized public behavior.

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at www.eajem.com. Manuscripts submitted via any other medium will not be evaluated. Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript is prepared and submitted in accordance with the journal's guidelines. Submissions that don't conform the journal's guidelines will be returned to the submitting author with technical correction requests.

Authors are required to submit the;

- Copyright Transfer Form,

- Author Contributions Form,

- and ICMJE Potential Conflict of Interest Disclosure Form (should be filled in by all contributing authors) during the initial submission. These forms are available for download at www.eajem.com

Title page: A separate title page should be submitted with all submissions and this page should include;

- The full title of the manuscript as well as a short title (running head) of no more than 50 characters,

- Name(s), affiliations and major degree(s) of the author(s)

- Grant information and detailed information on the other sources of support,

- The name, address, telephone (including the mobile phone number) and fax numbers and e-mail address of the corresponding author,

- Acknowledgement of the individuals who contributed to the preparation of the manuscript but do not fulfil the authorship criteria.

Abstract: An abstract should be submitted with all submissions except for letters to the editor. The abstract of Original Articles should be structured with subheadings (Aim, Materials and Methods, Results and Conclusion).

Keywords: Each submission must be accompanied by a minimum of three and a maximum of six keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations.

Manuscript Types

Original Articles: This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Materials and Methods (with subheadings), Results, Discussion, Study Limitations, Conclusion subheadings. Please check Table 1 for limitations for Original Articles.

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with the international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and statistical software that was used during the process must certainly be specified. Data must be expressed as mean±standard deviation when parametric tests are used to compare continuous variables. Data must be expressed as median (minimum-maximum) and percentiles (25th and 75th percentiles) when non-parametric tests are used. In advanced and complicated statistical analyses, relative risk (RR), odds ratio (OR) and hazard ratio (HR) must be supported by confidence intervals (CI) and p values.

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

INSTRUCTIONS TO AUTHORS

Editorial Comments: Editorial comments aim at providing brief critical commentary by the reviewers having expertise or with high reputation on the topic of the research article published in the journal. Authors are selected and invited by the journal. Abstract, Keywords, Tables, Figures, Images and other media are not included.

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.

Case Reports: There is limited space for case reports in the journal and reports on rare cases or conditions that constitute challenges in the diagnosis and treatment, those offering new therapies or revealing knowledge not included in the books, and interesting and educative case reports are accepted for publication. The text should include Introduction, Case Presentation, Discussion, Conclusion subheadings. Please check Table 1 for limitations for Case Reports.

Letters to the Editor: This type of manuscripts can discuss important parts, overlooked aspects or lacking parts of a previously published article. Articles on the subjects within the scope of the journal that might attract the readers' attention, particularly educative cases can also be submitted in the form of "Letter to the Editor". Readers can also present their comments on the published manuscripts in the form of "Letter to the Editor". Abstract, Keywords, Tables, Figures, Images and other media are not included. The text should be unstructured. The manuscript that is being commented on must be properly cited within the manuscript.

Scientific letter: Manuscripts with prior notification characteristics, announcing new, clinically important scientific developments or information are accepted as Scientific Letters. Scientific Letters should not include sub-headings and should not exceed 900 words. Number of references should be limited to 10 and number of tables and figures should be limited to 2.

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.

Tables

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

Figures and Figure Legends

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

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

INSTRUCTIONS TO AUTHORS

the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300DPI. To prevent delays in the evaluation process all submitted figures should be clear in resolution and large in size (minimum dimensions 100x100 mm). Figure legends should be listed at the end of the main document.

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)"

All references, tables and figures should be referred to within the main text and they should be numbered consecutively in the order they are referred to within the main text.

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

References

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:

Journal article: Lewin MR, Stein J, Wang R, Lee MM, Kernberg M, Boukhman M, et al. Humming is as effective as Valsalva's maneuver and Trendelenburg's position for ultrasonographic visualization of the jugular venous system and common femoral veins. Ann Emerg Med. 2007;50:73-7.

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.

Editor(s) as author: Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of 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/ncidodlElD/cid.htm.

REVISIONS

When submitting a revised version of a paper, the author must submit a detailed "Response to reviewers" that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be cancelled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial 30 day period is over.

PROOFS AND DOI NUMBER

Manuscripts accepted for publication are provided with a DOI number immediately after acceptance. Accepted manuscripts are copy-edited for grammar, punctuation, and format. Once the publication process of a manuscript is completed it is published online on the journal's webpage as an ahead of print publication before it is included in its scheduled issue. A PDF proof of the accepted manuscript is sent to the corresponding author and their publication approval is requested within 2 days of their receipt of the proof.

PERMISSIONS AND REPRINTS

Permission requests for reproduction of published content and reprint orders should be directed to the Editorial Office.

Please get in direct contact with the Editorial Office if you have any questions or comments regarding the journal.

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

Contents

Review

79 Can Acute Care Biomarkers Change Patient's Management in Sepsis?
Salvatore Di Somma, Luca Crisanti; Rome, Italy

Original Articles

86 Unintentional Accidents in the 0-6 Age Group: Evidence from Turkey
Ayhan Tabur; Diyarbakır, Turkey

93 Comparison of Emergency Medical Services Cases in Different Types of Mass Gathering Events Held Between 2015-2018 in Turkey
Hüseyin Koçak, İbrahim Tuncay; Çanakkale, İstanbul, Turkey

100 Short-Term Prognosis of Patients with Hyperpotassemia in the Emergency Department
Recep Yıldırım, Ertuğ Günsoy, Oktay Eray; Antalya, Van, Turkey

106 How Can We Detect Delirium Easier Among Oncologic Patients in the Emergency Department?
Mustafa Boz, Nalan Metin Aksu, Elif Öztürk, Mehmet Mahir Kunt, Ali Batur; Ankara, Turkey

114 Analysis of the Degree of Accuracy and Reliability of Emergency Medicine Residents in Interpreting Computed Tomography of the Abdomen
Sümeyye Tuğba Sarkı Cander, Şule Akköse Aydın, Vahide Aslıhan Durak, Murat Çetin, Deniz Sığırlı; Bursa, İzmir, Turkey

120 Diagnostic Accuracy of the Sonographic Ottawa Foot and Ankle Rules for Ankle and Foot Fractures in Emergency Department
Farhad Heydari, Loabat Adib, Saeed Majidinejad, Reza Azizkhani; Isfahan, Iran

126 Implementing a Simulation-Based Distance Learning Model: How to Facilitate High-Engagement Experiential Training While Reducing the Risk of Infectious Disease Transmission Amongst Healthcare Professionals
Héctor Alonso, Maria Soledad Holanda, Liébana Piedra, Ignacio Del Moral, Jose M. Maestre; Santander, Spain

132 Can Spesific Biomarkers Be Used to Enlighten the Major Mechanisms of Acute High Dose Diclofenac Sodium-Related Nephrotoxicity?
Sinem Doğruyol, İlker Akbaş, Abdullah Osman Koçak, Serpil Aygörmez, Habip Emrah Leylek, Sultan Tuna Akgöl Gür, Özge Ertener; Manisa, Bingöl, Erzurum, Kars, Balıkesir, İzmir, Turkey

138 Evaluation of Patients Admitted to the Emergency Department with the Suspect of Acute Renal Colic with the Modified STONE Score
Birdal Güllüpınar, Pınar Ayvat, Erden Erol Ünlüer, Serhat Koran; İzmir, İstanbul, Turkey

146 Emergency Physicians' Point of Care Ultrasonography (POCUS) Competency Assessment for the Diagnosis of Acute Appendicitis in Pediatric Cases
Hasan Atalar, Mustafa Keşaplı, Ömer Faruk Karakoyun, Adeviyye Karaca; Burdur, Antalya, Muğla, Turkey

Case Report

152 A Rare Cause of Intraabdominal Haemoraggy Ethiology: Retroperitoneal Haemoragic Cyst
Mehmet Buğra Bozan, Fatih Mehmet Yazar, Özlem Güler, Ömer Faruk Boran, Ayşe Azak Bozan; Kahramanmaraş, Turkey

Letters to the Editor

156 COVID-19: Questionable Seasonality
Sadaf Sheikh; Muscat, Oman

157 Point of Care Ultrasound in COVID-19 Pandemic
Sadaf Sheikh; Muscat, Oman

EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2022.21.2.1
Review
Eurasian J Emerg Med. 2022;21(2): 79-85

Can Acute Care Biomarkers Change Patient's Management in Sepsis?

Salvatore Di Somma[1,2], Luca Crisanti[2]

[1]Department of Medical-Surgery Sciences and Translational Medicine, Sant'Andrea Hospital, Sapienza University of Rome, School of Medicine and Psychology, Emergency Medicine, Rome, Italy
[2]Department of Emergency Medicine, Postgraduate School of Emergency Medicine, Sapienza University of Rome, Sant'Andrea Hospital, Rome, Italy

Abstract

Sepsis and septic shock have an enormous burden on healthcare systems, having more than 30 million people worldwide suffering from those diseases. As emergency providers we must be able to immediately recognize the presence of sepsis to improve the management of this disease and reduce its burden on patient's lives and on the emergency departments. Biomarkers can play an important role in this attempt. Laboratory tests could help both to identify the presence of sepsis at patients' arrival and to stratify the risk of progression to septic shock. A new biomarker in that regard is represented by Bioactive Adrenomedullin (BioADM), which mirrors vascular integrity, and is able to detect the physio pathological deterioration of the patients with sepsis that will progress into septic shock. Now, thanks to point-of-care testing devices, we are able to measure BioADM in whole blood in less than twenty minutes, which will help the physician making faster and more adequate therapeutical decisions beside patient's bed. The good news is that BioADM will also serve as a target for a monoclonal antibody that will counteract the vascular disfunction in septic shock. In conclusion, coupling BioADM with other biomarkers already routinely used such as procalcitonin and lactate we can immediately change patient's management in Sepsis improving our decision making and patient outcome

Keywords: Acute care biomarkers, sepsis, emergency

Introduction

There are more than 30 million people worldwide suffering from sepsis (1), and its incidence is even greater than other acute diseases such as cardiovascular and cancer ones (2). The mortality rate in ICU for patients with septic shock is estimated to be around 35% (3) and this high mortality rate may increase of 8% with every delayed hour of treatment (4).

As consequence we need to improve our diagnostic accuracy of sepsis in the emergency room (ER) to improve its earliest management and reduce its mortality.

The importance of improving the approach to patients presenting with infection in ER is not only related to the possibility that these subjects could be already suffering from sepsis and could suddenly deteriorate to septic shock, but it's also linked to the fact that, even when they survive form sepsis and are discharged from the hospital, these patients could experience severe consequences, such as: cognitive dysfunction, physical and psychological disabilities (5).

Following recent guidelines, emergency providers must then be able, starting from the triage, to immediately recognize the presence of sepsis in order to reduce the burden of the disease (6). Papers, also from our group (7,8) demonstrated that overcrowding of the emergency department is linked with high mortality rate and when compared with other several diseases, such as acute coronary syndrome or acute respiratory distress, sepsis showed the highest mortality rate in the emergency room.

Corresponding Author: Prof. Salvatore Di Somma, M.D., Department of Medical-Surgery Sciences and Translational Medicine, Sant'Andrea Hospital, Sapienza University of Rome, School of Medicine and Psychology, Emergency Medicine, Rome, Italy & Department of Emergency Medicine, Postgraduate School of Emergency Medicine, Sapienza University of Rome, Sant'Andrea Hospital, Rome, Italy
E-mail: salvatore.disomma@uniroma1.it ORCID ID: orcid.org/0000-0002-1717-6585

Received: 17.03.2022
Accepted: 23.05.2022

Cite this article as: Di Somma S, Crisanti L. Can Acute Care Biomarkers Change Patient's Management in Sepsis? Eurasian J Emerg Med. 2022;21(2):79-85.

Indeed, recent guidelines of the Surviving Sepsis campaign recommend to organize a specific pathway in the emergency department to deal with sepsis (6).

Previous guidelines on sepsis of 2016 (9) recommended to immediately stratify the severity of sepsis using the quick sequential organ failure assessment (qSOFA) score, while the new guidelines (6) are suggesting that qSOFA score is not adequate anymore in this attempt; recommending to immediately test blood lactate to decide to use or not antibiotics.

Lactate measurement is not a diagnostic tool for sepsis since it is mirroring organ dysfunction in the presence of septic shock (10); therefore, we need something else, before lactate rises, to properly diagnose Sepsis in ER and to stratify the risk of the patient to develop septic shock.

Our group recently published a paper that clearly shows that the standard diagnostic tool for sepsis is the culture positive for bacteria detection (11). The problem is that we cannot have a cultural positive result in the emergency room because it will take at least 24 hours, or even more to be obtained.

Biomarkers for Early Diagnosis and Risk Stratification of Sepsis in ER

As already demonstrated by several studies, the only biomarker that is linked with the high possibility to properly detect the presence of sepsis is procalcitonin (12,13). On the contrary, white blood cell count and C-reactive protein (CRP) are very unspecific biomarkers for the detection of sepsis (14).

In (Figure 1A) ROC curve for diagnosis of sepsis: white blood cell (WBC) area under the curve (AUC): 0.533, p=0.780; procalcitonin (PCT) AUC: 0.798, p<0.0001; CRP AUC: 0.720, p=0.001. In (Figure 1B) receiver operating characteristics (ROC) curve for outcome (in-hospital death) in total population: WBC AUC: 0.635, p=0.180; PCT AUC: 0.723, p<0.0001; CRP AUC: 0.538, p=0.239. T0, time of arrival in ED (14).

Consequently, many subjects could suddenly develop septic shock even though at ED arrival the clinical signs and laboratory testing were not able to detect it.

Could we be able to immediately detect the presence of sepsis upon the patient's arrival? This is what we are trying to achieve in the future, to help physicians to identify the presence of infection, sepsis and septic shock so that we could be able to stop the progression of the disease.

From physio pathological point of view, the mechanism that mirrors the transition from systemic infection to septic shock is due to an acute vascular dysfunction with loss of vascular integrity (15).

So, we need to have biomarkers that are able to detect the presence of ongoing severe vascular dysfunction as soon as possible in septic patient.

BioAdrenomedullin: A Biomarker of Vascular and Endothelial function and Utility in Sepsis

Bioactive adrenomedullin (BioADM) was discovered in 1993 by Kitamura et al. (16), it is a peptide that is present into the circulatory vessel and it is responsible for vascular integrity inside and outside the vessel and plays also a role in vasodilatation.

This was firstly demonstrated in animal models (17,18) and then confirmed in humans (19-21).

Table 1. Characteristics at baseline of patients with sepsis divided into Culture-negative and Culture-positive

Characteristics	CnS (n=449)	CpS (n=324)	Un p	Un OR
Patients untreated with antibacterials during their stay in ED*, n (%)	26 (6)	6 (2)	0.009	3.257 (1.325-8.009)
Median body temperature (°C), (IQR)	37.5 (36.6-38.2)	37.8 (36.7-38.2)	0.331	
Median mean arterial pressure (mmHg), (IQR)	86 (76-95)	85 (75-93)	<0.001	1.019 (1.009-1.029)
Median heart rate (beats/min), (IQR)	100 (90-110)	104 (78-120)	0.912	
Median respiratory rate (breaths/min), (IQR)	24 (20-28)	24 (21-32)	0.361	
Median Glasgow Coma Scale (IQR)	15 (15-15)	15 (15-15)	0.183	
Median white blood cell count x 1000/mm^3 (IQR)	12.5 (9.0-16.4)	13.4 (9.8-18.5)	0.025	0.806 (0.629-1.001)*
Biomarkers				
Median C-reactive protein (mg/L) (IQR)	81 (31-170)	127 (53-215)	<0.001	0.769 (0.678-0.872)
Median lactate (mg/dL) (IQR)	14 (9-19)	14 (10-21)	0.103	
Median procalcitonin (ng/mL) (IQR)	0.51 (0.16-2.43)	1.12 (0.29-9.51)	<0.001	0.698 (0.619-0.787)

*Log scale transformed.
CnS: culture negative sepsis, CpS: Culture positive sepsis, Un: Unstandardised, OR: Odds ratio, IQR: Interquartile, ED: Emergency department (Adjusted from Di Somma et al.)

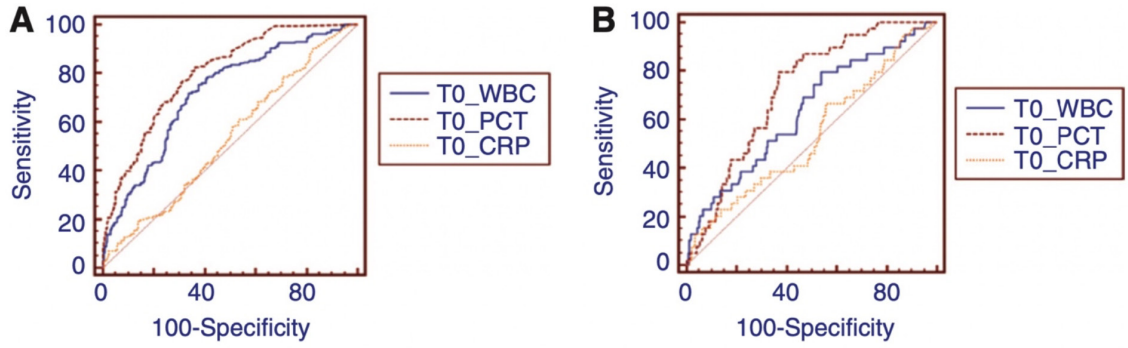

Figure 1. ROC curve for (A) diagnosis of sepsis and (B) prognosis of in-hospital death

ROC: Receiver operating characteristics, WBC: White blood cell, PCT: Procalcitonin, CRP: C-reactive protein

Role of bioactive adrenomedullin in the regulation of vascular function was shown in Figure 2 (22).

Using a new technology with immune sandwich assay (23) we are able to measure, *in vivo*, circulating levels of BioADM and its dynamic changes, mirroring the vascular dysfunction occurring in sepsis and we can really detect the physio pathological deterioration in septic patients and predict the progression to septic shock.

Scheme for biogenesis and measurement of bio-ADM was shown in Figure 3 (23).

First in the maturation process, the signal sequence is clipped off. The resulting pro-ADM is then proteolytically cleaved in four fragments (PAMP, proadrenomedullin NH2-terminal 20 peptide; MR-proADM, midregional proadrenomedullin; Adrenomedullin-Gly, C-terminally glycine-extended adrenomedullin; CT-proADM, C-terminal proadrenomedullin, also known as adrenotensin). The resulting C-terminally glycinated ADM is biologically inactive and is subsequently (but only partially) converted into the biologically active C-terminally amidated ADM (BioADM). Using highly specific monoclonal antibodies directed against the middle portion of ADM and the amidated C-terminus, BioADM can be detected with an immunometric assay (23).

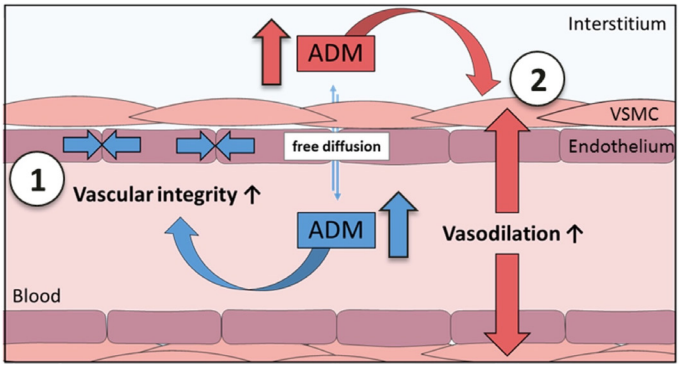

Figure 2. Role of bioactive adrenomedullin in the regulation of vascular function (22)

ADM: Adrenomedullin, VSMC: Vascular smooth muscle cells

This hypothesis has already been confirmed by our group (24) and by Chen and Li (25). Through the measurement of BioADM blood level in patients with the suspicion of sepsis at ED arrival. We were able to demonstrate that a value of bioADM greater than 70 pg/mL correlated with the severity of sepsis, the need for vasopressors and finally the progression to septic shock and death (24). After that study, multicentric studies, with other cohorts in other countries, have shown the same results (26-28). Therefore, the cut off of 70 pg/mL of bioADM should be considered as a marker for the severity of sepsis, predictor of septic shock and the need for vasopressors use.

Lately, in a small cohort, high circulating levels of BioADM were also correlated with organ failure and 30-days mortality in septic patients (29).

Bio-ADM cut-off of 70 pg/mL correlates with the severity of sepsis, the use of vasopressors and the septic shock as the cause of death (Figure 4) (24).

Furthermore, blood levels of BioADM are not affected by any previous antibiotic treatment, making it a very reliable biomarker.

In the same paper we also demonstrated, by monitoring BioADM levels from arrival for 7 days, that if there was a reduction of BioADM from high to low level, those patients showed a better prognosis (24), confirming that there is the possibility to reverse the negative outcome in these subjects.

This includes the concept that we can use this biomarker to monitor and evaluate the treatment efficacy.

Again, this was confirmed both by our preliminary study and through other multicentric studies (26,27).

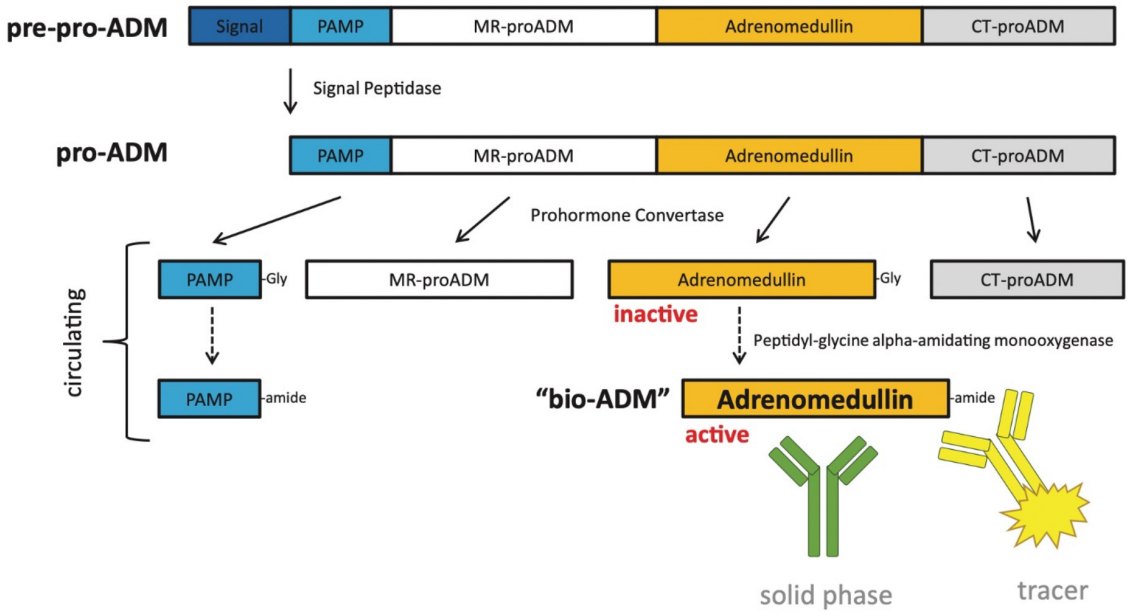

Figure 3. Scheme for biogenesis and measurement of BioADM (23)

BioADM: Bioactive adrenomedullin

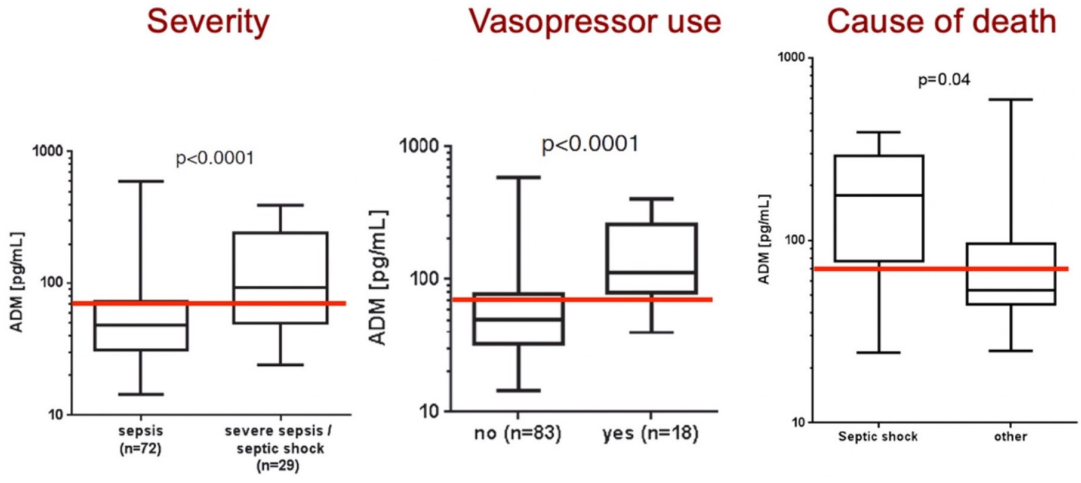

Figure 4. BioADM cut-off of 70 pg/mL correlates with the severity of sepsis, the use of vasopressors and the septic shock as the cause of death (24)

BioADM: Bioactive Adrenomedullin

BioADM medical utility in sepsis: prediction, diagnosis and monitoring of acute vascular dysfunction resulting in septic shock (Figure 5).

Utility of POCT Device for BioADM Evaluation

In the future we will use, as much as possible, the ultrasound point of care systems in the emergency room and point of care biomarkers devices in order to make a more appropriate and rapid decision making (30). This would be of great utility also in patients presenting with sepsis in order to start the best treatments as soon as possible.

Thanks to the POCT IB10 (Nexus Dx Inc., San Diego, CA, USA) device it's possible to measure BioADM levels in whole blood in less than 20 minutes, allowing ED physicians to make faster therapeutical decision in patients with sepsis and improve their outcome (Figure 6).

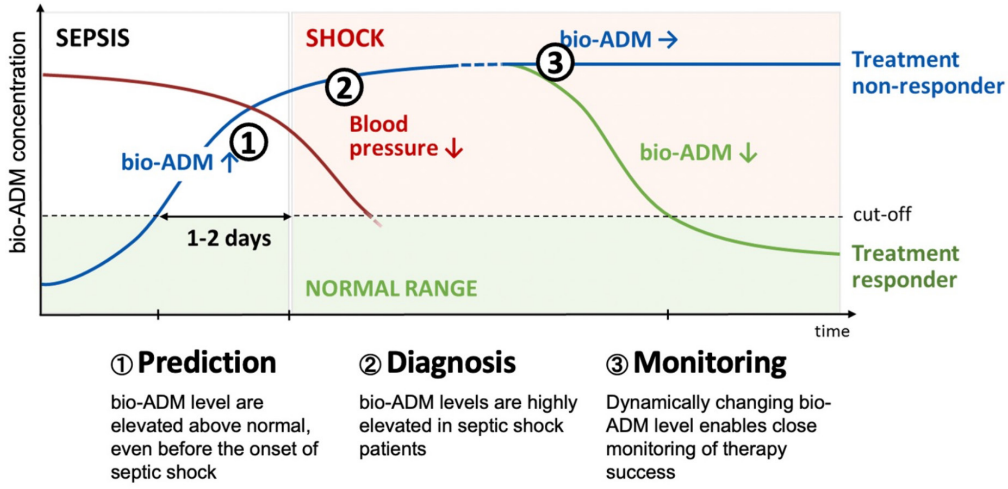

Figure 5. BioADM medical utility in sepsis: prediction, diagnosis and monitoring of acute vascular dysfunction resulting in septic shock

BioADM: Bioactive adrenomedullin

Since the value of IB 10 could be obtained 20 minutes after the arrival of patients in the emergency room, if the obtained result is greater than 70 pg/mL, the ED physician could have immediately important information on the patient's severity and make a specific decision in terms of therapeutical options and final disposition.

So, we would suggest that patients arriving to the ED with fever and risk factors, such as: hypertension, diabetes, kidney failure, they could be good candidates for BioADM testing, since they're at high risk for progression to septic shock.

From the recent guidelines (6), it is mandatory in patients with suspicion of sepsis to measure lactate, since patients with a lactate value greater than 2 mmol/L are at increased risk to develop septic shock. A recent paper shows that, when testing for BioADM and lactate (31), if both are elevated the mortality of patients with sepsis rises up to around 50%.

This supports the fact that we can use both biomarkers together to better understanding of the severity of our patient.

Figure 6. Nexus Dx Inc. IB10 device for poct BioADM testing (https://www.nexus-dx.com/nexus-ib10/)

BioADM: Bioactive adrenomedullin

Adrecizumab: A Novel Monoclonal Antibody for BioADM

The good news is that soon we will have a new drug option that could be taken into account during our therapeutical decisions. It has been developed a new monoclonal, Adrecizumab, that is able to restore the physiological function of BioADM on vessels.

The efficacy of anti-adrenomedullin antibodies in reducing mortality had already been demonstrated in 2013 through murine models (32).

Its mode of action is described in Figure 7, basically it manages to rise ADM concentration inside the vessels by translocating pre-existing ADM from the interstitial compartment. Furthermore, Adrecizumab seems to prevent ADM from being degradated and to prolong its half-life. In fact, a recent paper demonstrated that Adrecizumab is able to counteract the vascular dysfunction in septic shock (22).

Confirming this, Laterre et al. (33) recently showed how this drug improved the survival of patients with sepsis and a BioADM level greater than 70 pg/mL.

Therefore, in the future, it will be possible to use this monoclonal antibody in those patients that present in the emergency room with sepsis and a BioADM value greater than 70 pg/mL. This will improve their outcome by counteracting the vasculature damage before the patients goes to deteriorate into septic shock.

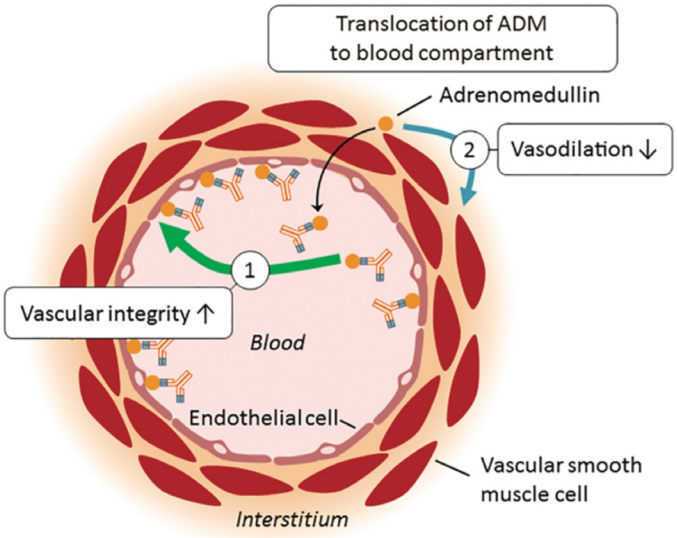

Figure 7. Mechanism of action of adrecizumab (19)

ADM: Adrenomedullin

Anyway, while we wait for the possibility of routinely using Adrecizumab, when we have a patient that seems to be stable, but his circulating BioADM is greater than 70 pg/mL, we could anticipate the start of vasopressors treatment in order to reduce the possibility of the patient to develop septic shock. Moreover, it would be possible to monitor BioADM for the following 7 days in order to verify the effect of the vasopressors early treatment.

Conclusion

Since every hour of delay in diagnosing of sepsis and septic shock in the emergency room is going to be linked with high mortality rates, we need new biomarkers for early detection of sepsis, beyond lactate. BioADM, that could also be measured by POCT devices on whole blood in 20 minutes, seems to be a very good new biomarker now available to reduce the burden of septic shock in the emergency room.

Finally, we would recommend using biomarkers in the emergency room really with care, since we do not need to treat the number, we need to treat the patients.

Ethics

Peer-review: Externally peer-reviewed.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395:200-11.
2. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Card Fail Rev. 2017;3:7-11.
3. Medam S, Zieleskiewicz L, Duclos G, Baumstarck K, Loundou A, Alingrin J, et al. Risk factors for death in septic shock: A retrospective cohort study comparing trauma and non-trauma patients. Medicine. 2017;96:e9241.
4. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34:1589-96.
5. Kempker JA, Wang HE, Martin GS. Sepsis is a preventable public health problem. Crit Care. 2018;22:116.
6. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47:1181-247.
7. Di Somma S, Paladino L, Vaughan L, Lalle I, Magrini L, Magnanti M. Overcrowding in emergency department: an international issue. Intern Emerg Med. 2015;10:171-5.
8. Valli G, Galati E, De Marco F, Bucci C, Fratini P, Cennamo E, Ancona C, Volpe N, Ruggieri MP. In-hospital mortality in the emergency department: clinical and etiological differences between early and late deaths among patients awaiting admission. Clin Exp Emerg Med. 2021;8:325-32.
9. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017;43:304-77.
10. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315:801-10.
11. Mearelli F, Barbati G, Spagnol F, Nunnari A, Castello LM, Lupia E, et al. The role of mid-regional proadrenomedullin in the differential diagnosis between culture-negative and culture-positive sepsis at emergency department admission. Biomedicines. 2022;10:357.
12. Wacker C, Prkno A, Brunkhorst FM, Schlattmann P. Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. Lancet Infect Dis. 2013;13:426-35.
13. Harbarth S, Holeckova K, Froidevaux C, Grau GE, Vadas L, Pugin J, et al. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. Am J Respir Crit Care Med. 2001;164:396-402.
14. Magrini L, Gagliano G, Travaglino F, Vetrone F, Marino R, Cardelli P, et al. Comparison between white blood cell count, procalcitonin and C reactive protein as diagnostic and prognostic biomarkers of infection or sepsis in patients presenting to emergency department. Clin Chem Lab Med. 2014;52:1465-72.
15. Ince C, Mayeux PR, Nguyen T, Gomez H, Kellum JA, Ospina-Tascón GA, et al. The endothelium in sepsis. Shock. 2016;45:259-70.
16. Kitamura K, Kangawa K, Kawamoto M, Ichiki Y, Nakamura S, Matsuo H, Eto T. Adrenomedullin: a novel hypotensive peptide isolated from human pheochromocytoma. Biochem Biophys Res Commun. 1993;192:553-60.
17. Nakamura K, Toda H, Terasako K, Kakuyama M, Hatano Y, Kangawa K, et al. Vasodilative effect of adrenomedullin in isolated arteries of the dog. Jpn J Pharmacol. 1995;67:259-62.
18. Hirata Y, Hayakawa H, Suzuki Y, Suzuki E, Ikenouchi H, Kohmoto O, et al. Mechanisms of adrenomedullin-induced vasodilation in the rat kidney. Hypertension. 1995;25(4 Pt 2):790-5.
19. Voors AA, Kremer D, Geven C, Ter Maaten JM, Mebazaa A, Butler J, et al. Adrenomedullin in heart failure: pathophysiology and therapeutic application. Eur J Heart Fail. 2019;21:163-71.
20. Cockcroft JR, Noon JP, Gardner-Medwin J, Bennett T. Haemodynamic effects of adrenomedullin in human resistance and capacitance vessels. Br J Clin Pharmacol. 1997;44:57-60.

21. Geven C, Kox M, Pickkers P. Adrenomedullin and adrenomedullin-targeted therapy as treatment strategies relevant for sepsis. Front Immunol. 2018;19;9:292.
22. Geven C, Bergmann A, Kox M, Pickkers P. Vascular effects of adrenomedullin and the anti-adrenomedullin antibody adrecizumab in sepsis. Shock. 2018;50:132-40.
23. Weber J, Sachse J, Bergmann S, Sparwaßer A, Struck J, Bergmann A. Sandwich immunoassay for bioactive plasma adrenomedullin. J Appl Lab Med. 2017;2:222-33.
24. Marino R, Struck J, Maisel AS, Magrini L, Bergmann A, Di Somma S. Plasma adrenomedullin is associated with short-term mortality and vasopressor requirement in patients admitted with sepsis. Crit Care. 2014;18:R34.
25. Chen YX, Li CS. Prognostic value of adrenomedullin in septic patients in the ED. Am J Emerg Med. 2013;31:1017-21.
26. Mebazaa A, Geven C, Hollinger A, Wittebole X, Chousterman BG, Blet A, et al. Circulating adrenomedullin estimates survival and reversibility of organ failure in sepsis: the prospective observational multinational Adrenomedullin and Outcome in Sepsis and Septic Shock-1 (AdrenOSS-1) study. Crit Care. 2018;22:354.
27. Lemasle L, Blet A, Geven C, Cherifa M, Mebazaa A, Gayat E, et al. Bioactive Adrenomedullin, Organ Support Therapies, and Survival in the Critically Ill: Results from the French and European Outcome Registry in ICU Study. Crit Care Med. 2020;48:49-55.
28. Caironi P, Latini R, Struck J, Hartmann O, Bergmann A, Maggio G, et al; ALBIOS Study Investigators. Circulating biologically active adrenomedullin (bio-ADM) predicts hemodynamic support requirement and mortality during sepsis. Chest. 2017;152:312-20.
29. Kim H, Hur M, Struck J, Bergmann A, Di Somma S. Circulating biologically active adrenomedullin predicts organ failure and mortality in sepsis. Ann Lab Med. 2019;39:454-63.
30. Di Somma S, Zampini G, Vetrone F, Soto-Ruiz KM, Magrini L, Cardelli P, et al. Opinion paper on utility of point-of-care biomarkers in the emergency department pathways decision making. Clin Chem Lab Med. 2014;52:1401-7.
31. Blet A, de Roquetaillade C, Hartmann O, Struck J, Mebazaa A, Chousterman BG; Adrenoss-1 study investigators. Added value of serial bio-adrenomedullin measurement in addition to lactate for the prognosis of septic patients admitted to ICU. Crit Care. 2020;24:69.
32. Struck J, Hein F, Karasch S, Bergmann A. Epitope specificity of anti-Adrenomedullin antibodies determines efficacy of mortality reduction in a cecal ligation and puncture mouse model. Intensive Care Med Exp. 2013;1:22.
33. Laterre PF, Pickkers P, Marx G, Wittebole X, Meziani F, Dugernier T, et al. Safety and tolerability of non-neutralizing adrenomedullin antibody adrecizumab (HAM8101) in septic shock patients: the AdrenOSS-2 phase 2a biomarker-guided trial. Intensive Care Med. 2021;47:1284-94.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2020.09821
Eurasian J Emerg Med. 2022;21(2): 86-92

Unintentional Accidents in the 0-6 Age Group: Evidence from Turkey

Ayhan Tabur

Clinic of Emergency Medicine, Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkey

Abstract

Aim: This study aims to analyze the data of children in the 0-6 age group who were exposed to unintentional accidents through a data set representing Turkey.

Materials and Methods: The variables used in the analysis were obtained from the "TurkStat Health Survey" micro data set for 2016. Although there are fifteen accident types in total, the data for the two accident types were excluded from the analysis because there was no data about them. Each accident element was analyzed by frequency, rate and difference analysis. In addition, the frequency of occurrence of each accident type per hundred thousand was calculated by using the sample.

Results: The first five accident types with the highest frequency of thirteen accident types, play-related injuries (8.7%), slips and falls (8.1%), insect bites and stings (3.4%), burns (2.9%) and foreign body aspiration (1.6%). The number of people exposed to thirteen accident types is 743 out of 2,272 people. 43% of the people exposed to the accident applied for treatment. The frequency of occurrence of all accidents per hundred thousand is 3,318.9.

Conclusions: According to the results of the research, the authorities directing the health policy should make an emergency action plan for the types of accidents with the highest frequency and the most sequelae.

Keywords: Unintentional accidents, sequelae, injury, Turkey

Introduction

Globally, every year, 973 million people are unintentionally injured each year while 4.8 million people die as a result of the injury. This accounts for 9% of the world's deaths, nearly 1.7 times the number of fatalities that result from human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), tuberculosis and malaria combined. Unintentional injuries including road traffic injuries, falls, burns and drowning account for about three-quarters of injury-related deaths. Injuries have a significant economic burden, as they impose heavy costs on the individual and society. The cost of injuries in India is estimated to be between 2-3% of the gross domestic product (GDP) (1).

In the United States, each year about 13,819 children and adolescents (0-19 years old) die from injuries, incurring a $21.95 billion cost to the social system. And more than three hundred thousand children and adolescents (0-19 years old) need hospitalization due to injuries, generating $32.14 billion cost (2).

Injuries are the leading cause of morbidity and mortality for children (3). Unintentional injury costs are high. According to a study conducted in the United States of America (USA) in 2012, injuries to children (including emergency treatment, hospitalization services and fatal) led to a cost of $92 billion costs and increased to $502 billion when the quality of life losses was taken into account. Non-fatal injuries account for 83% of these costs (4).

Injuries are divided into two, intentional and unintentional. Death and disability-adjusted life-years occur most often in low- and middle-income countries (more than 90%) (5). The top five causes of unintentional injuries published by the World Health Organization (WHO) are traffic accidents, drowning, poisoning, burns and falls. Other injuries include fractures, joint and muscle injuries, open wounds, and internal organ injuries. Unintentional injuries in children are affected in different ways by cultural, economic, living conditions and regional and demographic features (6).

Corresponding Author: Ayhan Tabur, M.D., Clinic of Emergency Medicine, Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkey
E-mail: ayhantabur@yaani.com ORCID ID: orcid.org/0000-0002-4743-766X

Received: 09.03.2020
Accepted: 01.09.2020

Cite this article as: Tabur A. Unintentional Accidents in the 0-6 Age Group: Evidence from Turkey. Eurasian J Emerg Med. 2022;21(2):86-92.

Every hour a child in the USA dies from an unintentional injury. About one in five child deaths is a result of unintentional injury. The sad side is that these deaths and injuries are largely preventable (7). In Table 1 below, in the Web-based Injury Statistics Query and Reporting System (WISQARSTM) USA-based and linked to Centers for Disease Control and) database (one of the most important databases on unintentional injuries (CDC) the types of accidents that lead to the most deaths are ranked by age groups.

In general, the burden of unintentional injuries among children is considerable all over the world, inflicting great economic losses on society, ranging from the US $516.938 to the US $9.550.704 per year (8). As a risk group, children, especially those under the age of 4, are exposed to higher rates of unintentional injuries. The direct and indirect economic costs of childhood unintentional injuries are mainly calculated by referring to medical treatment, length of stay (LOS) and loss of the healthy year (6).

To analyze the data for children exposed to unintentional accidents of the 0-6 age group through a data set representing Turkey's children is the main purpose of this study. The lack of a study based on data representing Turkey and examining all types of accidents together is the main motivator of this study.

Materials and Methods

In this study, "2016 Turkey's Health Research" micro data sets were used. The Health Questionnaire is conducted every 2 years by TURKSTAT and the most recent survey belongs to 2016. Its scope is households located in all settlements within the borders of Turkey. The population defined as institutional (population living in dormitories, hospitals, jails, rest homes, and soldiers) are out of coverage and also the residential places having less than 20 addresses are left out of coverage since it is thought that we would not be able to reach enough sample household number. The dataset was stratified and a two-step cluster sampling methodology was used. Nine thousand and four hundred and seventy household addresses were selected and researched to gather information about health indicators. The total number of observations in the data set is 23,606. In this study, there is information about 2,772 people in the 0-6 age group. There are questions for a total of 15 accident types. Since the question regarding carbon monoxide poisoning was not answered, this accident type could not be analyzed. In addition, since there is a lack of information about other accident types, they were excluded from the study.

Table 1. Leading causes of unintentional injury deaths, United States 1999-2015, all races, both sexes

Rank	Age groups			
	<1	1-2	3-4	5-6
1	Suffocation 3,968	Drowning 5,191	MV traffic 3,583	MV traffic 3,375
2	MV traffic 1,901	MV traffic 3,735	Drowning 2,352	Drowning 1,169
3	Drowning 868	Suffocation 1,814	Fire/burn 1,653	Fire/burn 988
4	Fire/burn 500	Fire/burn 1,545	Suffocation 570	Suffocation 285
5	Natural/environment 304	Pedestrian, other 1,271	Pedestrian, other 469	Other land transport 226
6	Unspecified 299	Natural/environment 403	Struck by or against 261	Pedestrian, other 217
7	Fall 249	Fall 387	Natural/environment 229	Struck by or against 138
8	Poisoning 241	Poisoning 358	Fall 217	Natural/environment 129
9	Other specified, classifiable 141	Struck by or against 313	Firearm 217	Fall 122
10	Struck by or Against 91	Unspecified 171	Other land transport 181	Poisoning 113

Source: https://webappa.cdc.gov/sasweb/ncipc/nfilead.html (Accessed in February 2020).
Data Source: National Center for Health Statistics (NCHS), National Vital Statistics System; WISQARSTM Produced By: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention

Results

Firstly, six variables (gender, hearing loss, vision loss, presence of mental retardation, speech delay, and attention deficit) included in the data set were subjected to differential analyzes according to accident types. The difference analysis was done with the t-test. Thirteen types of accidents were then tabulated in terms of frequency and rate analysis of exposure, age of exposure, whether they were treated after exposure, and whether there was any malaise or sequelae as a result of the treatment.

Difference analysis; In the analysis of differences, an answer was sought for the question of whether there are differences between the groups in terms of gender, hearing loss, vision loss, the presence of mental retardation, speech delay and attention deficit. No difference was found between all those with and without hearing loss and vision loss in terms of accident types ($p>0.05$).

"Does the exposure of children with and without delayed speech to all types of accidents differ?" The answer to the question differs only in terms of the following titles: children with speech delay are exposed to fewer accidents in accident types such as play-related injuries, slips and falls, insect bites and stings, burns and foreign body aspiration ($p<0.05$). The exposure of children with and without attention-deficit to the accident was examined in terms of all accident types. There are differences only in terms of slips and falls, burns and play-related injuries. Children who have attention deficit are exposed to fewer accidents in accident types such as slips and falls, burns and play-related injuries ($p<0.05$). Those with and without mental retardation were compared in terms of all accident types and no difference could be determined.

The answers to the question of whether the frequency of accident types varies according to the gender variable were examined in terms of thirteen types of accidents. Gender differences are only statistically demonstrable in terms of only two accident types. Girls [n=1,343, M=1.975 and standard deviation (SD): 0.15] are exposed to more insect bites and stings [t (2770)=2.275, p=0.023] than boys (n=1,429, M=1.96 and SD: 0.195) statistically. Furthermore, girls (n=1,343, M=1.93 and SD: 0.253) have more accidents due to more play-related injuries than boys (n=1,429, M=1.91 and SD: 0.289) [t (2770)=-2.243, p=0.025] statistically. The other eleven types of accidents do not differ by the gender variable.

The top five accident types with the highest frequency of thirteen accident types are play-related injuries (8.7%), slips and falls (8.1%), insect bites and stings (3.4%), burns (2.9%) and foreign body aspiration (1.6%). The number of people exposed to thirteen accident types is 743. Of these, 426 are boys and 317 are girls. 43% of the people exposed to the accident applied for treatment. The most common types of accidents that apply to treatment are slips and falls, burns, play-related injuries and insect bites and stings respectively. Those exposed to burning are the group that has to live mostly with sequelae. This group is followed by those who are exposed to slips and falls and play-related injuries. The rate of sequelae after the treatment is 3,3%. In order to provide an international comparison, the frequency of occurrence of all accidents per hundred thousand has been calculated and determined as 3,318.9 (Table 2).

The frequency of occurrence of thirteen accident types in the 0-6 age range is shown in Table 2. When the table is viewed in general, the age at which the play-related injuries are most common is the age of 5 and above. In the slip and fall group, the group above 2 years of age and below 3 years of age fell the most. In terms of insect bites and stings, those over 3 years under 4 years take the lead. In terms of burns and corrosive esophageal burns, those over 2 years under 3 years take the lead. Information on other types of accidents is detailed in Table 3.

Discussion

Accidents are still an important public health problem due to their frequent occurrence, leading to death and disability. Unsafe environmental conditions and unsafe behavior play an important role in accident formation (9). Children who are curious, active, very interested in their environment, but whose mobility skills are not fully developed, their cognitive and behavioral developments are not completed, and therefore lack of perception of possible risks is frequently exposed to accidents (10).

In a study conducted in Turkey, 12.6% of children were identified in the accident story (11). Since there were thirteen types of accidents in this study, the highest distribution is 8.7% with the play-related injury. The type of accident that has the lowest rate is a sport-related injuries with oesophagus and burns with a ratio of one per thousand. In many studies conducted in our country and in the world, the frequency of accidents in children is at most 1-4 years of age. It is an expected result that the frequency of the accident has increased due to the fact that the self-monitoring behavior in children under three years of age has not developed, the visual fields are not fully developed and the inability to accurately determine the direction in which the sounds come from in children under the age of five (10).

In addition to road injuries, falls and burns are the leading causes of injuries among the population under the age of seven. Burns and falls are typically commoners and more severe among

Table 2. Injuries in terms of gender, referral to treatment and sequelae

Accidental elements	Gender (n=2,772)				Other highlights (n=2,772)							
	Male	Male (%)	Female	Female (%)	I HaC +	II NC -	I/II	Per one hundred thousand	NAT	TAR	RS	SRR	SRR per hundred thousand
Play-related injuries	131	30.75	92	29	223	2,549	0.087	8,044.73	53	0.24	24	0.009	865.8
Slips and falls	118	27.7	90	28.4	208	2,564	0.081	7,503.61	101	0.49	25	0.009	901.88
Insect bites and stings	57	13.38	33	10.4	90	2,682	0.034	3,246.75	30	0.33	2	0.001	72.15
Burns	43	10.09	35	11	78	2,694	0.029	2,813.85	62	0.79	30	0.011	1,082.25
Foreign body aspiration	23	5.4	20	6.3	43	2,729	0.016	1,551.23	16	0.37	2	0.001	72.15
Cutting tool injuries	12	2.82	12	3.8	24	2,748	0.009	865.8	11	0.46	5	0.002	180.38
Drowning	11	2.58	12	3.8	23	2,749	0.008	829.73	9	0.39	0	0	0
Poisoning	9	2.11	10	3.2	19	2,753	0.007	685.43	18	0.95	0	0	0
Traffic accident	8	1.88	4	1.3	12	2,760	0.004	432.9	7	0.58	2	0.001	72.15
Nursery school injury	8	1.88	5	1.6	13	2,759	0.005	468.98	8	0.62	1	0	36.08
Electric shock	4	0.94	1	0.3	5	2,767	0.002	180.38	1	0.2	1	0	36.08
Sports injury	2	0.47	1	0.3	3	2,769	0.001	108.23	3	1	0	0	0
Corrosive esophageal burns	0	0	2	0.6	2	2,770	0.001	72.15	1	0.5	0	0	0
The overall total	**426**	**100**	**317**	**100**	**743**		**0.022**	**2,061.828**	**320**	**0.43**	**92**	**0.033**	**3,318.9**

HaC: Had an accident +, NC -: No accident, NAT: Number of applicants to treatment, TAR: Treatment applicant rate, RS: Remaining sequelae, SRR: Sequelae remaining rate

children (12). In this study, the most common accident types were play-related injuries (8.7%), slips and falls (8.1%), insect bites and stings (3.4%), burns (2.9%) and foreign body aspiration (1.6%).

According to the systematic review study conducted by Barcelos et al. (13) in 2017, it was determined that there were significant improvements in the results of many studies thanks to the programs to prevent burns. Burn injuries are a major public health problem for children (14). Burns is an important cause of injury for young children and it is the third most common cause of injury after accidents resulting in death in motor vehicle accidents and drownings. Burn injuries lead to prolonged hospital stays and increase care-related costs. Most burn injuries in children are most commonly seen in children between the ages of 0-4, and these injuries are mostly burn injuries caused by hot liquids (15). In this study, burn injuries were more common in children aged 2-4 compared to other age groups. The highest age group is 3 years old. Approximately three people out of 100 were exposed to burns. In 2010, a study conducted by Atak et al. (11) on children under the age of 5 confirmed that burns were the second most common type of accident causing injuries. In this study, burn was ranked fourth.

In our study, the rate of application to the health institution after the accident was found to be 43% as the average of all accident types. There are accident types with 100 percent application (sports injuries; three people) and very low accident types (such as play-related injuries and electric shocks; one per thousand). Everyone exposed to sports injuries applied to health institutions. Ninety-five out of every hundred poisoned people, eight out of every ten people exposed to a burning accident, six out of every ten people exposed to a nursery injury, almost six out of ten exposed to a traffic accident, one out of two exposed to an esophagus burn, one in two people exposed to esophageal burns and one in two exposed to falls (49%) applied to a health facility. The lowest application numbers are applications related to game injuries and electric shock and one in five people applied. Kılıç et al. (9) determined this rate as 55% in their study in 2019. In the study of Kurt and Aytekin (16), this rate was reported as 51%. In Kurt and Aytekin's (16) study, falls accounted for 45.9% of household accidents.

We do not have information regarding how many of the children have elbow, femur and humerus fractures at the end of each accident when applying to the health facility. In addition, the survey participants were not asked if they were hospitalized as a result of the accident and about the care costs. Despite this, some statements have been added

Table 3. Number of accidents by age groups

Accidental elements	Age ranges							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**Total**
Play-related injuries	9	24	33	33	43	33	48	223
Slips and falls	18	28	33	40	32	24	33	208
Insect bites and stings	8	8	12	17	19	9	17	90
Burns	1	16	29	21	4	6	1	78
Foreign body aspiration	2	11	10	12	0	6	2	43
Cutting tool injuries	1	1	3	6	6	4	3	24
Drowning	7	5	4	5	0	0	2	23
Poisoning	1	1	5	3	4	3	2	19
Traffic accidents	1	0	0	1	3	3	4	12
Nursery school injuries	0	1	2	0	3	5	2	13
Electric shocks	0	0	1	3	1	0	0	5
Sports injuries	1	0	0	0	1	1	0	3
Corrosive esophageal burns	1	0	1	0	0	0	0	2
Total age groups	**50**	**95**	**133**	**141**	**116**	**94**	**114**	**743**

1: 0-6 months, 2: less than 6 months-12 months, 3: over 1 year under 2 years, 4: over 2 years under 3 years, 5: over 3 years under 4 years, 6: over 4 years under 5 years, 7: 5 years and over

to the text by making use of the literature about the possible consequences of falling accidents by using the resources below. The most common cause of injury in children is falling. The sideways trend may lead to upper extremity fractures in order to protect himself/herself while falling. Most distal radius and elbows are affected by this injury. The frequency of elbow injuries is most common in preschool children. Supracondylar humerus fractures account for 60% of elbow fractures (17). Femur fractures due to falls are among the conditions that children of this age are exposed to. Femur fractures occur as a result of high falls or motor or bicycle accidents. This affects hospital stay time and costs (18). The most frequently injured area differs greatly by age. In another study, it was observed that elbow injuries were common in groups of 0-2 (mummy's boy), 3-6 (game boy) (19).

When the literature was analyzed, it was reported that boys were more often exposed to accidents than girls (9,20,21). In Laffoy's (21) study, 59.2% of the children who had a home accident were identified as boys. In the study of Yalaki et al. (20), this rate was found to be 52% for the boys. It was stated that boys are more frequently exposed to accidents than girls since they are more active and active (22). In this study, in terms of frequency and ratio, boys were injured more than girls in game-related injuries. However, on the T-test based on group averages, the average of boys was 1.9083 and the average of girls was 1.9315. Since $p<0.05$, the difference between group averages is significant. Girls with a high average are more likely to have game-related injury levels than boys. This finding reverses the general literature. This subject can be clarified with wider participation and multinational studies taking into account the geographical and cultural dimensions.

Study Limitations

Questions such as whether there were deaths as a result of the types of accidents were not asked in The Turkish Health Survey Data. Therefore, there was no general assessment of the fate of the people who suffered the accident. We only have information whether sequelae remain as a result of the treatments of the accident victims. There is also no information on the time of the accident and the factors that led to the accident. The Turkish Health Survey data does not include the result statements for sequela and injury related to accidents. For example, loss of hearing or vision due to an accident. As the participants were asked about conditions such as hearing loss, vision loss, mental retardation, speech delay and attention deficit, the statements regarding this condition were not associated with accidents and were not evaluated in the discussion section.

In addition, when the answers to the questions asked by 0-6 age group patients are examined, the answers to the questions related to the family, socio-economic status and household characteristics of each child are not included in the Turkish Health Survey data. Parents were asked separate questions. Questions about hearing loss, vision loss, mental retardation, speech delay and attention deficit were answered in binary groups as yes or no. In this respect, only the difference analysis could be

made with the available data. The causes and consequences of accidents were not asked with detailed questions, and impact and relationship analyzes could not be carried out as there is no data available.

Costa Riberio et al. (23) examined accidents under two headings as proximal determinants and distal determinants in their compilation study in 2019. The proximal determinants identified were: age and sex of children, and ethnicity. Mediating variables were variables such as parental behavior and surveillance. Parental employment and socioeconomic status were identified as distal determinants. In health research data, there are no variables that question ethnicity, mediators and the socio-economic level of parents.

Conclusion

Injury is an important child health problem that requires adequate attention and funding. Improved data collection infrastructure and evidence-based resource allocation for surgical services can aid in addressing pediatric injury, which is a major public health problem.

The frequency and preventability of unintentional injury underscore the importance of child and teen injury as a public health problem. We know what works, but there are a variety of challenges to overcome. Because injuries are common, they may be thought of as inevitable and "just part of growing up." There are many causes of injury, and each poses different risks and has different prevention strategies that change as children grow and develop. We cannot and should not aim to prevent every bump and bruise. However, we can identify the behaviors and environments most likely to contribute to severe, devastating, or fatal injuries and teach children, teens, and parents how to avoid them.

Based on WHO's wound prevention strategies, policymakers need to develop an action plan to prevent unintentional injuries. The first precaution should be to determine the deaths due to accidents. The action plan should give priority to accident elements with the highest frequency and develop a financial burden calculation methodology for each accident type. Furthermore, strategies for intervention and prevention of unintentional injuries must be developed rapidly. For example, road safety improvements, the use of bicycle helmets, child seats and smoke alarms can significantly reduce the number of accidental injuries.

Ethics

Ethics Committee Approval: Since this study is a secondary dataset, ethics committee approval is not required.

Informed Consent: Since this study is a secondary dataset, informed consent was not obtained.

Peer-review: External peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

References

1. Prinja S, Jagnoor J, Sharma D, Aggarwal S, Katoch S, Lakshmi PVM, et al. Out-of-pocket expenditure and catastrophic health expenditure for hospitalization due to injuries in public sector hospitals in North India. PloS One. 2019;14:e0224721.
2. Wang Z, Chen H, Yu T, Liu S, Hu, M. Status of injuries as a public health burden among children and adolescents in China: A systematic review and meta-analysis. Medicine. 2019;98:e17671.
3. Helton JJ, Weaver NL. Unintentional child injury in child welfare placements. Child Abuse Negl. 2020;99:104231.
4. Spicer R, Lawrence B, Miller T. 112 Cost of child and adolescent injury in the United States: by age group, cause, and payer. Injury Prevent. 2016;22:A42.
5. Chandran A, Hyder AA, Peek-Asa C. The global burden of unintentional injuries and an agenda for progress. Epidemiologic Rev. 2010;32:110-20.
6. Lao Z, Gifford M, Dalal K. Economic cost of childhood unintentional injuries. International J Prevent Med. 2012;3:303.
7. Dellinger A, Gilchrist J. Leading causes of fatal and nonfatal unintentional injury for children and teens and the role of lifestyle clinicians. Am J Lifestyle Med. 2019;13:7-21.
8. Jiang X, Zhang Y, Wang Y, Wang B, Xu Y, Shang L. An analysis of 6215 hospitalized unintentional injuries among children aged 0-14 in northwest China. Accid Anal Prev. 2010;42:320-6.
9. Kılıç E, Bayazit T, Gündoğdu G, Koşaroğlu NE, Sümer H. Sivas İl Merkezi Kreş ve Anaokulu Çocuklarında Ev Kazası Geçirme Sıklığı ve Etkileyen Faktörler. Cumhuriyet Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi. 2019;4:14-25.
10. İnce T, Yalçın SS, Yurdakök K. Çocukluk çağında ciddi kaza sıklığı ve risk faktörleri. Çocuk Sağlığı ve Hastalıkları Dergisi. 2014;57:173-82.
11. Atak N, Karaoglu L, Korkmaz Y, Usubütün S. A household survey: unintentional injury frequency and related factors among children under five years in Malatya. Turk J Pediatr. 2010;52:285.
12. Nwanna-Nzewunwa O, Ngamby MK, Cox J, Feldhaus I, Motwani G, Monono ME, et al. Epidemiology and cost of pediatric injury in Yaoundé, Cameroon: a prospective study. Eur J Trauma Emerg Surg. 2020;46:1403-12.
13. Barcelos RS, Del-Ponte B, Santos IS. Interventions to reduce accidents in childhood: a systematic review. Jornal de Pediatria. 2018;94:351-67.
14. Tekin R, Yolbaş İ, Selçuk CT, Güneş A, Özhasanekler A, Aldemir M. Onbeş Yillik Çocuk Yanik Hastalarinin Değerlendirilmesi. Ulusal Travma ve Acil Cerrahi Dergisi. 2012;18:514-8.
15. Toon MH, Maybauer DM, Arceneaux LL, Fraser JF, Meyer W, Runge A, Maybauer MO. Children with burn injuries-assessment of trauma, neglect, violence and abuse. Journal Inj Violence Res. 2011;3:98.
16. Kurt FY, Aytekin A. 0-6 yaş grubu çocuklarda ev kazaları. Sağlık Bilimleri ve Meslekleri Dergisi. 2015;2:22-32.
17. Acar E, Memik R. Surgical Treatment Results in Pediatric Supracondylar Humerus Fractures. Eurasian J Emerg Med. 2017;19:25-9.
18. Korucu İH. Treatment of school-age children with femoral shaft fracture: spica castıng versus titanium elastic nail fixation. Selçuk Med J. 2016;32:80-3.
19. Bombacı H, Ülkü K, Adıyeke L, Kara S, Görgeç M. Çocuk yaralanmaları, nedenleri ve önlemler. Acta Orthop Traumatol Turc. 2008;42:166a173.

20. Yalaki Z, Tasar MA, Kara N, Dallar Y. Measuring the Awareness of Home Injuries in Families with a Low Socioeconomic Status. J Acad Emerg Med. 2010;9:129.
21. Laffoy M. Childhood accidents at home. Irish Med J. 1997;90:26-7.
22. Baysal SU. Çocukluk çağında kazalar ve yaralanma kontrolü. Turkiye Klinikleri Pediatric Sciences-Special Topics. 2006;2:64-78.
23. Costa Riberio MG, Rocha Paula AB, Rocha Bezerra MA, Rocha S, Dantas Avelino FVS, Teles De Oliveira Gouveia M. Social determinants of health associated with childhood accidents at home: An integrative review. Revista Brasileira de Enfermagem. 2019;72:265-76.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.34392
Eurasian J Emerg Med. 2022;21(2): 93-9

Comparison of Emergency Medical Services Cases in Different Types of Mass Gathering Events Held Between 2015-2018 in Turkey

Hüseyin Koçak[1], İbrahim Tuncay[2]

[1]Department of Disaster Medicine, Institute of Health Sciences, Bezmialem Vakıf University, İstanbul; Çanakkale Onsekiz Mart University, Faculty of Health Sciences, Department of Emergency Aid and Disaster Management, Çanakkale, Turkey
[2]Departmant of Orthopedic and Trauma, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Turkey

Abstract

Aim: The aim of the study is to evaluate the Emergency Medical Services (EMS) cases in some mass gatherings held in Turkey between the years of 2015-2018 and to compare the patient presentation rate (PPR) and transport to hospital rate (TTHR) rates of different types of mass gatherings (MGs).

Materials and Methods: The research is a descriptive cross-sectional epidemiological study. The population of the study consists of 112 EMS records of the Commemoration Events of the Çanakkale Land Warfare (CEÇLW), Zeytinli Rock Festival (ZRF), Summer Deaflympics (DEAFLYMPICS) and European Youth Olympic Winter Festival (EYOF) organizations held in Turkey between the years of 2015-2018.

Results: The hours of 12:00 p.m. - 05:59 p.m. (34.0%, n=161). 57.4% (n=272) of the cases were due to medical 474 EMS cases were examined in the study. 49.5% (n=235) of the cases were in DEAFLYMPICS and 57.6% (n=273) of the cases were male. The mean age of the cases was 30.3±16.5 (minimum: 0, maximum: 92). Most cases occurred between reasons. According to the triage codes, 57.7% (n=153) of the cases were green, 32.3% (n=153) were red and 15.8% (n=75) were yellow. When the results of the cases were analyzed, 54.0% (n=256) of the cases were transferred to hospital, 20.7% (n=98) were on-site intervention and 14.1% were refusal of transfer.

Conclusion: As a result, differences in PPR and TTHR rates are observed in different types of MG.

Keywords: Ambulance, emergency medical services, EMS, mass gathering, PPR, TTHR

Introduction

Although mass gatherings (MGs) are common throughout the world, there is no universal definition yet (1-4). According to the World Health Organization, MGs are defined as the gathering of people in a planned or unplanned manner in an amount that exceeds the limits of emergency plan and the response resources of a society (5-13). The most common noncommunicable health problems seen in MGs are headache, abdominal complaints, abrasion/lacerations, orthopedic discomfort, eye injury, syncope/dizziness, burns, chest pain, heat-related injuries, respectively (14). Patient presentation rate (PPR) is seen in the range of 0.12 to 0.90 in MGs. Among the leading causes of mortality during MGs are stampede and heat related diseases (15). Alcohol and drug use are common in many festivals. Conditions requiring medical intervention are 10% more in such events.

In Lund et al.'s (16) study, transport to hospital rate (TTHR) value for the study of Bledsoe et al. was 0.61, 0.54 for Lund et al. (16), 0.22 for Luther et al., and 0.19 for Munn et al. In another study, 15 MGs held in South Australia were analyzed, and PPR was found to be 0.48 (n=146) while TTHR was found to be 0.04 in the MG activities where the total number of participants was 303,500 (17). Minor problems (headache, neck pain, fluid retention, etc.) were among the most common health problems at 41.1% (n=60) (17). This is followed by sprains, injuries and insect bites at 26.7% and major injuries (fractures and lacerations) at 13.7% (17). Almost 90% of the patient admissions took place in the activities where alcohol sales were allowed (17). In the same study, while

Corresponding Author: Prof. Dr. Hüseyin Koçak, Ph.D., Department of Disaster Medicine, Institute of Health Sciences, Bezmialem Vakıf University, İstanbul; Çanakkale Onsekiz Mart University, Faculty of Health Sciences, Department of Emergency Aid and Disaster Management, Çanakkale, Turkey
E-mail: acilafet@hotmail.com ORCID ID: orcid.org/0000-0001-8377-1828
Cite this article as: Koçak H, Tuncay İ. Comparison of Emergency Medical Services Cases in Different Types of Mass Gathering Events Held Between 2015-2018 in Turkey. Eurasian J Emerg Med. 2022;21(2):93-9.

Received: 11.01.2021
Accepted: 30.04.2021

the average temperature of the activities was between 20º-25º, there were fewer patient applications in the activities above 25º than the others, contrary to the information in the literature (17).

This is the second scientific research on MGs conducted in Turkey. It is important in terms of presenting measures such as PPR and TTHR for medical cases which occurred in different types of MGs held in Turkey to the world literature for the first time. Within the scope of the study, four different types of mass gathering activities are compared with each other and with similar studies in the world.

The aim of the research is to evaluate the EMS cases in some MGs held in Turkey between the years of 2015-2018 and to compare the PPR and TTHR rates of different types of MGs.

Materials and Methods

The research is a descriptive cross-sectional epidemiological study. It is designed as a retrospective record research. Within the scope of the study, medical case records kept by 112 ambulance service on accidents and injuries, which occurred in some mass gathering events between 2015-2018, were evaluated.

Population of the Research

Health directors were interviewed about EMS planning and preparation works for Commemoration Events Çanakkale Land Battles (CEÇLW), Hearing Impared Summer Olimpics (DEAFLYMPICS) and European Youth Olympics Festival (EYOF) within the context of information about the population. Since no special preparation was made for Zeytinli Rock Festival (ZRF), no information was obtained (Table 1).

Characteristics of Selected Mass Gatherings

CEÇLW is held annually as a commemoration event in the Gallipoli peninsula of Çanakkale between April 24th-25th. In the CEÇLW, activities are organized at different points of the peninsula at the same time or in consecutive time periods. People of all ages come to the activities. An important part of the participants is 12-18 or 65+ years old. During the event, a massive physical exertion is made in some sections. Very Important Personel (VIP) and Very Very Important Personel (VVIP) people also attend the ceremonies. Therefore, a much different and comprehensive preparation is required than usual. Participants begin to move to Gallipoli on the morning of April 24th. Therefore, health measures start on April 23rd and take place on the field exactly on April 24th at 06:00 a.m. It occurs in the open ground with approximately 7-8 hours of sleep and rest during the night connecting the 24th of April to the 25th April. Around 10,000 people from different age groups from Australia and New Zealand attend the events (Table 1). At the Australian and New Zealand Army Corps (ANZAC) ceremonies, the ANZAC soldiers who died in the First World War are commemorated by performing the Dawn Service on the morning of the 25th of April. After the Dawn Service, participants climb a pathway towards the Long Pine monument (Table 1). Çanakkale 112 ambulance service takes health measures with pedestrian National Medical Rescue Teams (NMRT) for about 2 km. The ceremonies end on April 25th at 08:00 p.m.

Zeytinli Rock Festival (ZRF) is an event that usually young people attend by the sea with tent accommodation. In this event, health services in the area are provided by private ambulance companies. However, in emergency cases, Balıkesir 112 ambulance service intervenes and enables patients to be transferred to the nearest health facility. The events were organized as 3 days in 2014 and 5 days in 2018 (Table 1).

EYOF is an important sporting event held every two years with the participation of 50 European countries. EYOF events, in which athletes between the ages of 14-18 participate, are held in the form of summer and winter festivals (18). The EYOF, organised in Erzurum between 11th-18th February 2017, was held with a total of 1,311 participants and over 10 thousand audience, including 675 athletes from 34 different countries, 436 administrative and technical personnel, 120 VIP guests and 80 referee boards (Table 1) (19). In the EYOF held in Erzurum, alpine discipline, biathlon, cross-country skiing, snow skiing, ski jumping, curling, ice hockey, speed skating, figure skating sports were performed.

A total of eight thousand people including three thousand athletes and technical committees and five thousand spectators from 97 countries participated in DEAFLYMPICS held between 18th-30th July 2017 in Samsun (Table 1) (20). The Olympics were held in eight different districts of Samsun. The European Youth Olympic Festival is an important sporting

Table 1. The distribution of the participant numbers of some mass gatherings held in Turkey between 2015-2018 (Ankara 2019)

	2015	2016	2017	2018
CEÇLW (2x4=8 days)[1]	50,000	10,000	10,000	10,000
ZRF (5 days)[2]	100,000	150,000	-	-
DEAFLYMPICS[3] (13 days)	-	-	8,000	-
EYOF[4] (8 days)	-	-	13,000	-

[1]The data were taken from the authorities responsible for emergency health organization.
[2]The data were taken from biletix.com which sells tickets for events.
[3]The data were taken from the official site of the event. Access: March 15th, 2019; http://www.deaflympics2017.org/tr/samsun-deaflympics-2017-sona-erdi-detay/282
[4]The data were taken from the official site of the event. Access: March 15th, 2019; https://www.eyof2017erzurum.org/sayfa/detay/kapanis-basin-toplantisi-gerceklestirildi/253
CEÇLW: Commemoration Events Çanakkale Land Battles; DEAFLYMPICS: Hearing Impared Summer Olimpics, EYOF: European Youth Olympics Festival; ZRF: Zeytinli Rock Festival

event held every two years with the participation of 50 European member countries. EYOF events, in which athletes between the ages of 14th-18th participate, are held in the form of summer and winter festivals (18). Sixty emergency ambulances, one helicopter ambulance, four NMRT teams were assigned for the festival. In addition, 16 health cabins were created in the olympic areas where the olympics would be played (21). International and Turkish Sign Language Training was provided to all healthcare professionals within the scope of the event (22). The staff who knew the sign language were assigned in the hospital emergency departments.

Application of the Research

The data were obtained through the General Directorate of the Health Information Systems of the Ministry of Health of the Republic of Turkey. The data recorded in the General Directorate Emergency Health Automation System was converted to Excel format and sent to the researcher via external memory and e-mail. The data received in Excel format was given as seven separate and different pages, respectively: (1) case detail, (2) application information, (3) medication information, (4) diagnostic information, (5) material information, (6) measurement information, (7) rejection information.

The data extracted by the experts were examined by the researcher and the data that were the subject of the study were transferred to the database created in SPSS version 22.0 program (IBM Corp., Armonk, NY, USA).

Data Collection and Editing

For EMS cases in DEAFLYMPICS and EYOF MGs, all the records encoded as ODD55 and ODD25 were transferred to the database prepared in SPSS 22.0 program. The data of the cases in CEÇLW and ZRF were not created with a standard coding. Therefore, the data finding process was made according to the case address. The keywords of "Eceabat, marina, mimosa cafe, health boat, lonepine, heliport, conkbayırı, Kireçtepe, 57th regiment walk, tent hospital, anzac/Anzac bay, simulation center, VIP, monument and camping area" were scanned for CEÇLW between April 24th-25th and the data obtained were used. It was seen that there was no special record for the event in ZRF. For this reason, scanning the keywords of "Rock, Rack, Festival, Zeytinli, Concert, Tent, Camping Area, Rak, Altınkum Beach" constituted the data obtained.

The data in seven different pages in Excel were combined in the database prepared in SPSS 22.0 program by using the search page (CTRL+F) with Case ID numbers.

Statistical Analysis

Frequency Analysis: Frequency distribution between dependent and independent variables was taken for the descriptive analysis of the study. Tables were usually created based on the type of activity for comparison. The mean, standard deviation (SD), median, minimum and maximum values of the descriptive statistics of some variables were calculated.

Rate Calculations: In the research, PPR and TTHR rates were calculated both for MGs types and for total.

Patient Presentation Rate (PPR): It is the main criterion in the evaluation of health services in MGs. It is defined as the number of patients applying for health services among 1,000 participants of an event (23,24).

Transportation to Hospital Rate (TTHR) (24): It is the calculation of the rate of patients who are transferred to a hospital by an ambulance during a MGs among 1,000 participants. The number of patients and injured people transferred to the hospital/ number of participants x 1.000

Research Permissions and Ethics

Permission was obtained from the Non-Interventional Research Ethics Committee of University of Bezmialem Vakif with the decision number 15/233, dated 15.08.2018. Permission was obtained from the Ministry of Health with the letter number 75730711, dated 14.12.2017.

Results

Four hundred and seventy-four cases in four different types of MGs were examined within the scope of the research. In the study, the cases with ambulance intervention were 49.5% (n=235) in DEAFLYMPICS, 22.6% (n=107) in CEÇLW, 15.2% (n=107) in ZRF, 12.7% (n=60) in EYOF. The mean age of the study population is 30.3±16.5, [minimum (min): 0, maximum (max): 92]. In the cases examined in the study, age ranges with the highest number of participants were 18-34 in the CEÇLW at 41.1% (n=44); 18-34 in the DEAFLYMPICS at 60.4% (n=142), 18-34 in the EYOF at 56.7% (n=34), 18-34 in the ZRF at 73,6%. 57.6% (n=273) of the total cases were between the ages of 18-34. 57.6% (n=273) of the total cases were between the ages of 18-34 and 23.6% (n=112) were between the ages of 35-64. The age range of 13.3% (n=63) of the cases were 0-17 and 5.5% (n=26) were 65 and older.

Following the call, the mean time period before arrival to the case was 9.3 minutes (min) (SD=5.7, median=9.1) for ZRF, 1.6 min. for DEAFLYMPICS, 3.4 min. for EYOF and 8.3 min. for CEÇLW. In the research, it was seen that 34.0% (n=161) of the cases took place between the hours of 12:00 and 5:59 p.m., 28.3% (n=134) between 6:00 p.m. and 11:59 p.m., 26.6% (n=126) between 06:00 a.m. and 11:59 a.m., 11.2% (n=53) between 12:00 p.m. and 05:59. When the incidence hours of the cases were analyzed according to the activity types, the time period in which the cases

were seen most frequently was between 06:00 a.m. - 11:59 a.m. at 39.3% (n=42) in CEÇLW; 12:00 a.m. - 5:59 p.m. at 32.8% (n=77) in DEAFLYMPICS; 12:00 a.m. - 5:59 p.m. at 61.7% (n=37) in EYOF; 6:00 p.m. - 11:59 p.m. at 44.4% (n=32).

When the cases were examined according to the incident locations, 76.6% (n=82) of the cases in CEÇLW occurred in a field, 41.7% of the cases in DEAFLYMPICS occurred in a dormitory, 21.7% of the cases seen in EYOF (n=13) occurred in a hotel, 86.1% (n=62) of the cases seen in ZRF occurred on the street.

When the cases were examined according to the triage codes, 51.7% (n=254) of the cases were green, 32.3% (n=153) of the cases were red, 15.8% (n=75) of the cases were yellow and 0.2% of the cases were black. When the triage codes of the cases were analyzed according to activity types, 56.1% (n=60) of the cases in CEÇLW were code green, 25.2% (n=27) were code red and 18.7% (n=20) were code yellow. The triage codes of the cases in DEAFLYMPICS were 47.2% (n=111) green, while 36.6% (n=86) were red and 16.2% (n=38) were yellow. The triage codes of the cases in EYOF were 48.3% (n=29) green, 35.0% (n=21) red and 16.7% (n=38) yellow. When the triage codes of the cases in ZRF were examined, 62.5% of the cases were green code, 26.4% (n=19) were red code, 9.7% (n=7) were yellow code and 1.4% (n=1) were black code (Table 2).

When the results of the cases were analyzed, 54.0% (n=256) of the cases were transferred to hospital, 20.7% (n=98) were on-site intervention, 14.1% were refusal of transfer, 3.6% (n=17) were transfer for medical examination and 0.8% (n=4) were transfer between hospitals.

PPR values in the study are 1.3 for CEÇLW (average of 2015-2018), 18.1 for DEAFLYMPICS, 7.1 for EYOF and 0.3 for ZRF. TTHR values are 0.7 for CEÇLW, 13.3 for DEAFLYMPICS, 5.1 for EYOF and 0.2 for ZRF (Figure 1).

Considering the distribution of the cases according to ICD10 diagnostic codes, the most common pre-diagnoses were successively symptoms, signs and abnormal symptoms (nausea and vomiting, dizziness) at 22.3% (n=98), injury, poisoning and other consequences of some external causes at 19.2% (n=84), accidents at 14.4% (n=63), circulatory system diseases at 9.8% (n=43), musculoskeletal system and ligament tissue diseases at 9.6% (n=42), mental and behavioral diseases at 6.8 (n=30) and respiratory system diseases at 5.5% (n=24). The most common cases in CEÇLW were soft tissue trauma at 9.7% (n=7), hypotension at 6.9% (n=5), angina pectoris at 6.9% (n=5) and multi trauma at 5.5% (n=4). In DEAFLYMPICS, the most common cases were Soft Tissue Trauma at 18.3% (n=43), nausea and vomiting at 6.4% (n=15), lower extremity injuries at 5.1% (n=12), pain at 5.1% (n=12). In EYOF, 28.3% of the cases were multi trauma, 28.3% of them were soft tissue trauma and 5% (n=3) were upper extremity injuries. In ZRF, 20.8% (n=15) of the cases were mental and behavioral disorders due to alcohol use, 12.5% (n=9) were conversion, 4.2% (n=3) mental and behavioral disorders due to drug intake.

Discussion

Four hundred and seventy-four cases in four different types of MGs were examined within the scope of the research. In the MGs examined during the research (2015-2018), the most cases are in DEAFOLIMPICS with 49.5% (n=235). In the study, 54.0% (n=256) of the cases were transferred to the hospital. When the cases were examined according to the triage codes, 51.7% (n=254) of the cases were green, 32.3% (n=153) of the cases were red, 15.8% (n=75) of the cases were yellow and 0.2% of the cases were black.

In a study on the Emergency Health Services (EHS) records of 79 MG events between 2009 and 2011, the mean age of the patients was 32.1 (SD=16.8) (10). The mean age of the patients at the 2002 FIFA World Cup in Japan was 30±17 (25). The mean age of those receiving health care in University Games was 27 (between 14-70) (26). The mean age of the current study (30.3±16.5) shows similarity with the information in the literature. Nineteen percent

Table 2. The distribution of 112 ambulance cases by triage codes in some mass gatherings held in Turkey between 2015-2018 (EHAS, Ankara 2019)

	CEÇLW	DEAFLYMPICS	EYOF	ZRF	Total
	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)
Code red	27 (25.2)	86 (36.6)	21 (35.0)	19 (26.4)	153 (32.3)
Code yellow	20 (18.7)	38 (16.2)	10 (16.7)	7 (9.7)	75 (15.8)
Code green	60 (56.1)	111 (47.2)	29 (48.3)	45 (62.5)	245 (51.7)
Code black	-	-	-	1 (1.4)	1 (0.2)
Total	107	235	60	72	474

CEÇLW: Commemoration Events Çanakkale Land Battles; DEAFLYMPICS: Hearing Impared Summer Olimpics, EYOF: European Youth Olympics Festival, ZRF: Zeytinli Rock Festival, EHAS: Ministry of Health National Database

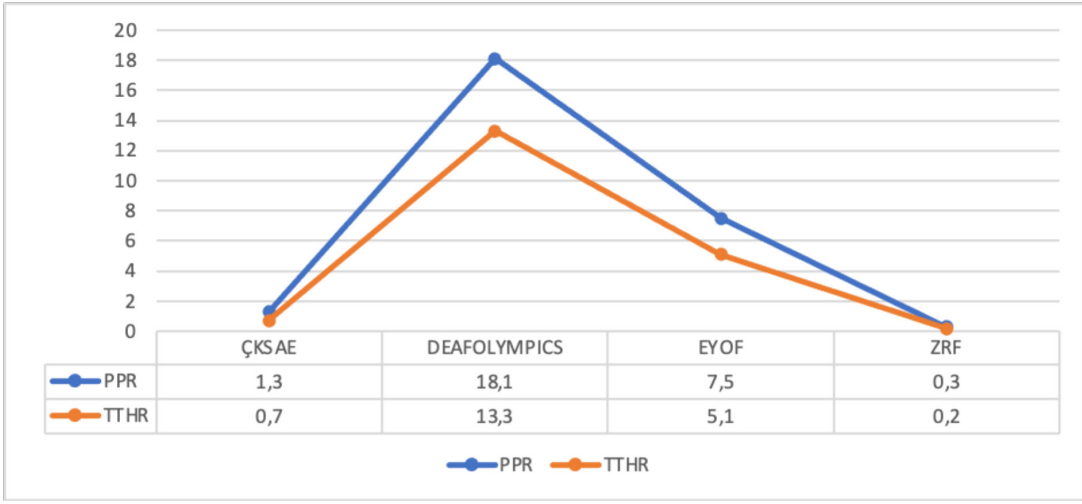

Figure 1. Patient presentation rate (PPR) and transport to hospital rate (TTHR) rates of different types of mass gatherings

ÇKSAE: Commemoration Events of the Çanakkale Land Warfare, DEAFLYMPICS: Hearing Impared Summer Olimpics, EYOF: European Youth Olympics Festival, ZRF: Zeytinli Rock Festival

of the cases that occurred in Milan 2015 EXPO were under the age of 18 (14). In the research, 57.6% of the cases are between the ages of 18-34. This is because DEAFLYMPICS and EYOF sports games are the activities for young people. In addition, the music type of ZRF mostly appeals to people in this age group. Likewise, both Turkish and Australian citizens mainly bring young people to CEÇLW in order to create national feelings among them. For all these reasons, a large part of the population in MGs is also considered to be in the 18-34 age range.

It was observed that the cases were most frequently experienced between 12:00 a.m. and 4:00 p.m. in Swiss Wrestling and Alpine Games (27). In a 4-year analysis of Formula 1 Singapore Night Races, it was found that the most cases (66.6%) occurred between 5:00 p.m. and 10:00 p.m. during the MGs (28). In the research, it was seen that approximately 80% of the cases in ZRF took place between the hours of 6:00 p.m. and 05:59 a.m. These hours are between the active start and end hours of the concert. When it is compared, the findings of the DEAFLYMPICS (32.8%) and EYOF (61.7%), which are the sport activities of this study, show similarities with the information in the literature.

Following the call, the mean time period before arrival to the case was 9.3 min (SD=5.7, median=9.1) for ZRF, 1.6 for DEAFLYMPICS, 3.4 for EYOF and 8.3 for CEÇLW. The time period of arrival was 8.3 min for CEÇLW and 9.3 min for ZRF. Sport events were in a better position than the other MGs types because of the high standards of health services provided by the olympic committee. These periods being shorter than others are thought to be due to the presence of ready teams in each hall and considered to be related to the fact that sports competitions were held in fixed places.

During the 2015 EXPO in Milan, 1% of the patients transferred to the hospital were code red, 29% were code yellow, and 70% were code green (4). In the research, 32.3% of the cases were code red and 15.8% were code yellow. In EYOF and DEAFLYMPICS, which are sports events, cases with code red were 35.0% and 36.6%, while the cases with code yellow were 16.0% and 16.2%, respectively. Twenty-five point two percent of the cases in CEÇLW, which is a commemoration event, were code red and 18.7% were code yellow (Table 2). MG types are similar among themselves in terms of triage codes. However, it differs with the work done in Milan. The reason for this is thought to be the staff's lack of knowledge or inadequacy of sensitivity in using the triage codes in Turkey. The fact that approximately 1/3 of the total cases were red code suggests that there were deficiencies in terms of applications and interventions. For example, in one case (Case 2), the preliminary diagnosis of the wrist and crush injury of the hand was entered as a code red. Another case (168th case) diagnosed as an acute respiratory infection was entered as a code red. In this way, the red coded cases are abnormally high.

In the research, 54.0% of the cases were transferred to hospitals. 61.3% of the cases in DEAFLYMPICS, 33.6% of the cases in CEÇLW, 66.7% of the cases in EYOF, 50.0% of the cases in ZRF were transferred to hospitals. Mobile hospitals were established on the Gallipoli peninsula during CEÇLW. Therefore, it is natural that the number of the transfer to hospitals is lower than others.

It is stated in the literature that PPR values in many MGs were between 0.5 and 2.0 (10). In 15 MGs in South Australia, PPR was 0.48 and TTHR was 0.04 (17). PPR was found to be 2.1 in the research conducted on Nigeria University Games (26). In the

research at Georgetown University, PPR value was found to be 0.39 for 184 MGs activities between 2011-2016 (29).

As a commemoration activity, the mean PPR value was 1.3 for CEÇLW. When the PPR values of the CEÇLW were examined by years, PRR values were estimated to be 0.3 for 2015, 1.9 for 2016 and 2017, and 3.3 for 2018. The PPR value was found to be 0.3 in ZRF. These results are similar to common PPR values in the literature. The PPR value was 0.39 for 184 MGs activities examined by Georgetown University and held between 2011-2016, and it was 1.2 for 2002 FIFA World Cup in Japan.

For sports activities, the PPR value of DEAFLYMPICS was 18.1, while it was 7.1 in EYOF. It appears to be higher in terms of PRR value compared to both literature and the other MGs in the study (Figure 1).

The TTHR rate was found to be 0.7 in CEÇLW. In a study conducted by Ranse et al. (30) on music festivals, TTHR was calculated to be 0.35. As a rock concert, the TTHR rate was calculated to be 0.2 in ZRF. In VIM, the highest TTHR rate was found to be 0.58 and the lowest TTHR rate was 0.09. The mean TTHR was found to be 0.04 in 15 MG in South Australia.

It is difficult to compare transportation to hospital rates, as there are different studies in the literature and the injured may have applied to emergency services or other polyclinics not only with ambulances but also with their own means (16).

Study Limitations

Firstly, since the research is a retrospective research, there may be deficiencies in the data due to the lack of records. Secondly, there might be deficiencies in the records of minor injuries and interventions in MGs activities. Thirdly, the research data are taken from the Ministry of Health national database (EHAS). For this reason, deficiencies due to not transferring some information in written forms to the digital database are among the limitations of the research. Fourthly, the only data that were used within the scope of the research was from the Ministry of Health. Fifthly, the healthcare interventions of the medical teams of private healthcare institutions or teams/participants, and interventions in mobile hospitals are not covered by the research. Sixthly, the lack of knowledge about the importance of the data records of healthcare professionals who recorded the cases, and the non-standardized entry technique may be another limitation of the study.

Conclusion

Four hundred and seventy-four emergency health care cases were examined in the study. It is seen that there are differences in PPR and TTR rates according to activity types in mass meetings. In the study, the majority of the cases are green-coded, while red-coded cases are rarely seen. PPR value varies according to the activity type. In sports organizations, cases are intervened faster. It is seen that more than half of the cases were transferred to the hospital. The records of 112 ambulance cases should be made with a special coding through the introduction of special criteria for some MGs, especially in terms of duration and number of participants, by the Ministry of Health. For MGs (festivals, memorial ceremonies, etc.) which are organised regularly, it is necessary to determine standardized processes at local and regional level and to support health services which would be provided on a regular basis. In order to distinguish emergency health services, especially for concerts and festivals, from ordinary life, a different coding must be used and recorded in the database. A legal infrastructure should be established for health services to be provided for MGs in Turkey.

Ethics

Ethics Committee Approval: Bezmialem Vakif University Non-invasive Clinical Researches Ethics Committee was approved this study (decision no: 2011-KAEK-42, date: 15.08.2017).

Informed Consent: This study is designed as a retrospective record research.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Design: H.K., İ.T., Data Collection or Processing: H.K., İ.T., Analysis or Interpretation: H.K., İ.T., Literature Search: H.K., İ.T., Writing: H.K., İ.T.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Murray V, Soomaroo L. Disasters at mass gatherings: lessons from history. PLoS Currents. 2012;4:RRN1301.
2. Wallis L, Smith W. Emergency Preparedness: Mass Gatherings. In: Nurbeam T, Boylan M, editors. ABC of Prehospital Emergency Medicine. West Sussex, UK: Johns Wiley & Sons Ltd; 2016. p. 190-4.
3. Molloy MS, Sherif Z, Natin S, McDonnell J. Management of Mass Gatherings. In: Koenig KL, Schultz CH, editors. Koenig and Schultz's Disaster Medicine Comprehensive Priciples and Practices Disaster Medicine Comprehensive Priciples and Practices. First. USA: Cambridge University Press; 2010. p. 228-50.
4. Marino P, Albergoni E, Andreassi A, Chiodini G. Mass gatherings in Italy: a study from the 2015 Milan Expo. J Health Soc Sci. 2016;1:91-8.
5. Tam JS, Barbeschi M, Shapovalova N, Briand S, Memish ZA, Kieny MP. Research agenda for mass gatherings: A call to action. Lancet Infect Dis. 2012;12:231-9.

6. Arbon P. Planning medical coverage for mass gatherings in Australia: What we currently know. J Emerg Nurs. 2005;31:346-50.
7. Aljohani M, Kennedy KE. Mass gatherings. In: Keystone JS, Freedman DO, Kozarsky P, Connor, Bradley CA, Nothdurft HD, editors. Ciottone's Disaster Medicine. 2nd ed. China: Elsevier Inc.; 2015. p. 968-74.
8. Wilder-Smith A, Steffen R. Mass Gatherings. 2nd ed. Travel Medicine: Third Edition. Elsevier Inc.; 2012. p. 357-9.
9. Soomaroo L, Murray V. Weather and environmental hazards at mass gatherings. PLoS Currents. doi: 10.1371/4fca9ee30afc4
10. Locoh-Donou S, Guofen Y, Welcher M, Berry T, O'Connor RE, Brady WJ, et al. Mass-gathering medicine: A descriptive analysis of a range of mass-gathering event types. Am J Emerg Med. 2013;31:843-6.
11. Demott JM, Hebert CL, Novak M, Mahmood S, Peksa GD. Characteristics and resource utilization of patients presenting to the emergency department from mass gathering events. Am J Emerg Med. 2018;36:983-7.
12. Brown JF, Smith JG, Tataris K. Medical management of mass gatherings. In: Cone DC, Brice JH, Delbridge TR, Myers JB, editors. Emergency Medical Services: Clinical Practice and Systems Oversight, Clinical Aspects of EMS. 2nd ed. West Sussex, UK: John Wiley and Sons, Ltd.; 2015. p. 264-71.
13. Koçak H, Çalışkan C, Sönmezler MŞ, Eliuz K, Küçükdurmaz F. Analysis of Medical Responses in Mass Gatherings: The Commemoration Ceremonies for the 100th Anniversary of the Battle of Gallipoli. Prehosp Disaster Med. 2018;33:288-92.
14. Alquthami AH, Pines JM. A Systematic review of noncommunicable health ıssues in mass gatherings. Prehosp Disaster Med. 2014;29:1-9.
15. Steffen R, Bouchama A, Johansson A, Dvorak J, Isla N, Smallwood C, et al. Non-communicable health risks during mass gatherings. Lancet Infect Dis. 2012;12:142-9.
16. Lund A, Callaghan CW, Turris SA, Munn MB, Rabb H. On the Way Out: An Analysis of Patient Transfers from Four Large-Scale North American Music Festivals Over Two Years. Prehosp Disaster Med. 2019;34:72-81.
17. Anikeeva O, Arbon P, Zeitz K, Bottema M, Lund A, Turris S, et al. Patient Presentation Trends at 15 Mass-Gathering Events in South Australia. Prehosp Disaster Med. 2018;33:368-74.
18. Önder HA, Batal S. Yerel Yönetimlerin Uluslararası Spor Organizasyonlarındaki The Role of Local Governments in International Sport Organizations (EYOF 2017 - Erzurum Metropolitan Municipality Example). Atatürk Üniversitesi Sosyal Bilimler Enstitüsü Dergisi. 2018;22:1053-74.
19. EYOF. Kapanış Basın Toplantısı Gerçekleştirildi. [Internet]. Available from: http://www.eyof2017erzurum.org/sayfa/detay/kapanis-basin-toplantisi-gerceklestirildi/253 (Cited 2019 March 5).
20. Deaflympics. Samsun DEAFLYMPICS 2017 Sona Erdi. [Internet]. Available from: http://www.deaflympics2017.org/pt/samsun-deaflympics-2017-sona-erdi-detay/282 (Cited 2019 February 15)
21. DHA. Sağlık Bakanlığı Olimpiyatlara Hazır [Internet]. hürriyet.com.tr. Available from: http://www.hurriyet.com.tr/saglik-bakanligi-olimpiyatlara-hazir-40524003 (Cited 2019 February 15).
22. Doğan H. Samsun, 2017 Deaflympics'e Hazır [Internet]. milliyet.com.tr. Available from: http://www.milliyet.com.tr/samsun-2017-deaflympics-e-hazir-istanbul-yerelhaber-2100314/ (Cited 2019 February 15).
23. Lund A, Turris SA, Bowles R, Ii EMA, Steenkamp M, Hutton A, et al. Mass-gathering Health Research Foundational Theory: Part 1 - Population Models for Mass Gatherings. Prehosp Disaster Med. 2014;29:648-54.
24. Ranse J, Clined G, Clinepi G, Hutton A, Keene T, Lenson S, et al. Health service ımpact from mass gatherings: a systematic literature review. Prehosp Disaster Med. 2017;32:71-7.
25. Morimura N, Katsumi A, Asai Y, Ishii N, Ishihara T, Koido Y, et al. Analysis of Patient Load Data From the 2002 FIFA World Cup Korea/Japan. Prehosp Disaster Med. 2016;19:278-84.
26. Ogunbunmi PA, Adeyinka AO, Sanya AO, Amanor-Boadu SD, Olapade-Olaopa EO, Omisanjo OO, et al. On-Site Physicians at a Major Sporting Event in Nigeria. Prehosp Disaster Med. 2016;21:40-4.
27. Hostettler-Blunier S, Müller N, Haltmeier T, Hosner A, Bähler H, Neff F, et al. Public Medical Preparedness at the "Swiss Wrestling and Alpine Games 2013": Descriptive Analysis of 1,533 Patients Treated at the Largest 3-Day Sporting Event in Switzerland. Emerg Med Int. 2017;1-6. doi: 10.1155/2017/9162095
28. Ho WH, Koenig KL, Quek LS. Formula One Night Race in Singapore: A 4-Year Analysis of a Planned Mass Gathering. Prehosp Disaster Med. 2014;29:489-93.
29. DeGeorge L, Sarna N, Ordway E, Reid M, Baird A, Nable J. EMS Resource Utilization at College Campus Mass Gathering Events. J Coll Emerg Med Serv. 2018;1:24-30.
30. Ranse J, Lenson S, Keene T, Luther M, Burke B, Hutton A, et al. Impacts on in-event , ambulance and emergency department services from patients presenting from a mass gathering event : A retrospective analysis. Emerg Med Australas. 2018;1-6. doi: 10.1111/1742-6723.13194

EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2021.60243
Original Article
Eurasian J Emerg Med. 2022;21(2): 100-5

Short-Term Prognosis of Patients with Hyperpotassemia in the Emergency Department

Recep Yıldırım[1], Ertuğ Günsoy[2], Oktay Eray[3]

[1]Clinic of Emergency Medicine, Alanya Training and Research Hospital, Antalya, Turkey
[2]Clinic of Emergency Medicine, Van Training and Research Hospital, Van, Turkey
[3]Department of Emergency Medicine, Akdeniz University Hospital, Antalya, Turkey

Abstract

Aim: Although hyperkalemia is a common encountered electrolyte disorder in the emergency room, there is little information in the literature regarding its clinical results. In this study, the short-term prognoses of patients who applied to the emergency department for any reason and were found to have hyperkalemia were investigated.

Materials and Methods: This retrospective cohort study was carried out in a tertiary care university hospital emergency department by using the data provided by a hospital information management system (HIMS) in a year period. The 1st week and 28th day survivals of the patients who applied to the emergency department for any reason and were found to have hyperpotassemia (K >5.11 mg/dL) were evaluated. The relationship between potassium values at the first admission of patients with hyperkalemia and hospitalization or intensive care admissions, age, gender, hemodialysis needs, chronic kidney disease (CKD) and acute kidney injury (AKI), and survival were investigated.

Results: In the study, the results of 18,582 serum potassium samples were evaluated. Among the 2,715 hyperkalemia samples, 532 (19.5%) false potassium elevations and 363 (9%) repeat patients were measured. These samples were excluded from evaluation. Information of seven patients could not be reached and they were excluded from the study. Hyperpotassemia results of 1934 patients were included in the final analysis. It was found that 130 (6.7%) of the patients died within seven days, and 245 (12.7%) died within 28 days. In the study, 7-day and 28-day day mortality of patients who developed AKI, needed hemodialysis, who were hospitalized or located in intensive care unit were found to be significantly higher ($p<0.001$ for each). There was no statistical difference at 7th and 28th days between patients with CKD and those without CKD. It was found that AKI for patients, hyperpotassemia was associated with hospitalization, death and hemodialysis.

Conclusion: Patients with hyperkalemia accompanying AKI carry a risk in terms of mortality and other adverse prognoses. This risk has been found to be weaker in CKD. Hyperkalemia creates a serious risk even in hyperpotassemia close to normal value.

Keywords: Hyperpotassemia, hyperkalemia, emergency department

Introduction

Potassium abnormalities (hypopotassemia-hyperkalemia) can be seen in many patients admitted to the emergency department with various complaints and symptoms (1). Potassium is an electrolyte that is vital for cell functions. Potassium must be present in the blood at a certain concentration (3.5-5.0 mEq/L). Serum potassium values other than these values are defined as "serum potassium abnormality" (2). In the studies conducted in the related literature, potassium blood level abnormality was found in 13-15% of the patients who were hospitalized and followed up (3). As is known, potassium abnormality may not always be due to a clinical pathology (4). Causes such as laboratory measurement errors, analyzer and kit problems, and inappropriate blood sampling may be the cause of potassium abnormalities (5). Potassium abnormality may be asymptomatic in patients, but it may also lead to various conditions ranging from nausea-vomiting, paresthesia, heartbeat abnormalities to cardiac blocks due to conduction disturbances and sudden cardiac death (6). Therefore, patients with potassium abnormalities presenting to the emergency department should be diagnosed quickly and

Corresponding Author: Prof. Oktay Eray, M.D., Department of Emergency Medicine, Akdeniz University Hospital, Antalya, Turkey
E-mail: oktayeray@akdeniz.edu.tr ORCID ID: orcid.org/0000-0002-1643-6007

Received: 29.06.2021
Accepted: 17.08.2021

Cite this article as: Yıldırım R, Günsoy E, Eray O. Short-Term Prognosis of Patients with Hyperpotassemia in the Emergency Department. Eurasian J Emerg Med. 2022;21(2):100-5.

treatment should be initiated as soon as possible (7). Limited data are available on the prevalence, etiology and clinical outcomes of these patients with high severity (8,9). Most of these data are about patients who are hospitalized and followed up, and the epidemiology and clinical results of emergency room admissions are limited (10). This observational study was planned to analyze information about the prevalence, mortality, demographic characteristics, hospitalization, intensive care admission, hemodialysis numbers and rates of patients who were admitted to a tertiary emergency service in a one-year period and were found to have high potassium level.

Materials and Methods

Study Population

This observational study was carried out by using the data provided by a hospital information management system (HIMS) of a tertiary care university hospital emergency department in a year period (2016). Samples with high serum potassium level (K >5.11 mEq/L) were determined and included in the study. No kit and autoanalyzer changes were made in the central biochemistry laboratory within a year where the study data were analyzed. Since the upper limit of the normal value range of the serum potassium measurement device used by the Biochemistry Laboratory was 5.10 mEq/L, values of 5.11 mEq/L and above were evaluated as hyperkalemia and were included in the study. The files of the patients were scanned via HIMS.

Exclusion criteria of the study:

1. Serum potassium values in blood samples taken repeatedly from the same patient on the same day,

2. Patients with pseudo-potassium abnormalities in the control samples because the results of the patients with serum potassium abnormalities are not compatible with the clinical findings.

Data Collection

The seven-day and 28-day mortality information was investigated and detected from "Death Notification System". Seven-day and 28-day mortality data were determined separately. This questioning covers a period of 28 days from the date the patient admitted to the hospital with serum potassium abnormality. The data of the patients included in the study regarding hospitalization, admission to the intensive care unit and whether they underwent hemodialysis were determined by HIMS scanning. If CKD patients developed AKI, they were excluded from the CKD group and included in the AKI group.

It was determined that serum potassium values were studied from 18,582 samples between 01/01/2016 and 31/12/2016. Hyperpotassemia was detected in 2,715 (14.6%) of 18,582 samples. Two hundred and forty-two (8.9%) serum potassium samples from 2,715 hyperkalemia samples were excluded from the study because they were duplicate samples taken from the same patient on the same application. Five hundred and thirty-two (19.5%) (2.8% of all samples) measurements in which the control serum potassium level was studied before medical treatment were considered to be incompatible with the patient's clinical findings were not considered as true hyperpotassemia and were not included in the data set. Seven (0.2%) serum potassium samples were excluded from the study because the patients' information could not be obtained (foreign patients). As a result, the data of 1934 (10.4% of all samples) confirmed hyperkalemia patients were evaluated in the study (Figure 1).

Demographic characteristics, potassium levels, AKI, CKD, Hemodialysis, 7-day mortality, 28-day mortality, numbers and percentages of hospital and intensive care admissions of hyperkalemia patients (Table 1).

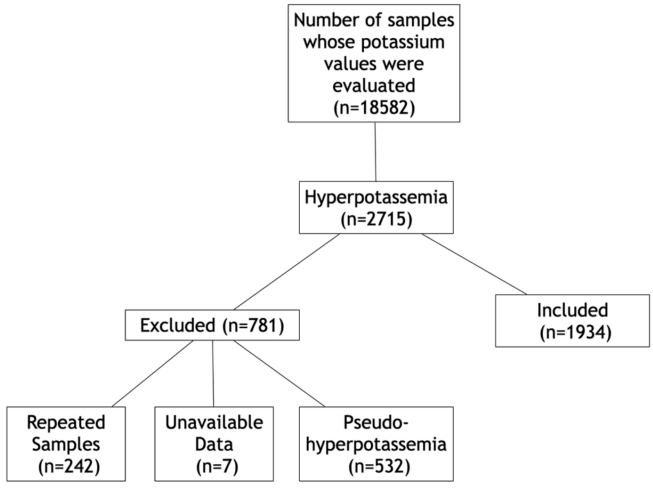

Figure 1. Scheme of emergency admissions with hyperkalemia

Table 1. Demographic characteristics	
Patients Included	**(n=1,934)**
Female/male	863/1,071 (44.6%)
Average age	61.6 (SD: 18.94)
Serum K levels	5.4 mEq/L (IQR: 0.56)
Acute kidney injury	297 (15.4%)
Chronic kidney disease	386 (20%)
Hemodialysis	218 (11.3%)
7-day mortality	130 (6.7%)
28 days of morality	245 (12.7%)
Hospital admission	820 (42.4%)
Intensive care admission	228 (11.8%)
SD: Standard deviation, IQR: Interquartile range, n: Number	

Gender distribution of hyperkalemia patients (1934 patients in total); 863 (44.6%) were female, 1,071 (55.4%) were male. In hyperkalemia patients, the lowest age was 1, the highest age was 115, and the mean age was 61.6 [standard deviation (SD): 18.94]. In the hyperpotassemia patient group, the mean age was 62.6 (SD: 19.14) in female group, and 60.7 (SD: 18.74) in male group.

The graph showing the distribution of serum potassium values of patients with hyperkalemia (It is seen that serum potassium values are not normally distributed and there is a density between 5.1 mEq/L and 5.5 mEq/L) (Figure 2).

When the serum potassium values in our study were examined, it is seen that the lowest serum potassium value was 5.11 mEq/L, the highest serum potassium value was 9.52 mEq/L, and the median serum potassium value was 5.40 mEq/L [interquartile range (IQR): 0.56].

Of the 1,934 patients included in the study, 297 (15.4%) had AKI, 386 (20.0%) had CKD, and 218 (11.3%) were admitted to hemodialysis. Moreover, it was found that 130 (6.7%) of the patients with hyperpotassemia died within seven days, and 245 (12.7%) died within 28 days. In addition, it was determined that 820 (42.4%) of the patients included in the study were hospitalized and treated, and 228 (11.8%) of these patients were admitted to intensive care.

Results

When we examine 130 patients who died in seven days, it was observed that 64 (49.2%) patients had AKI (21.5% of 297 patients with AKI) (Table 2). It was also observed that 4.0% (66 patients) of patients without AKI died within seven days. The frequency of AKI in patients with hyperkalemia who died within a week was statistically significant, which was higher than those who did not die ($p<0.001$). It was seen that 36 (27.6%) of 130 patients who died within a week were taken on hemodialysis (16.5% of 218 patients who received hemodialysis). It was found that 5.5% of the patients (94 patients) who were not treated with hemodialysis died within seven days. The frequency of hemodialysis was statistically significant, which was higher in patients who had hyperkalemia and died within a week than those who did not die ($p<0.001$).

It was found that 23 (17.6%) of 130 patients who died within a week had CKD (6.0% of 386 patients with CKD), 6.9% of patients without CKD (107 patients) died within seven days. There was no statistical difference between those with CKD and those without CKD in patients with hyperkalemia who died within a week ($p=0.503$).

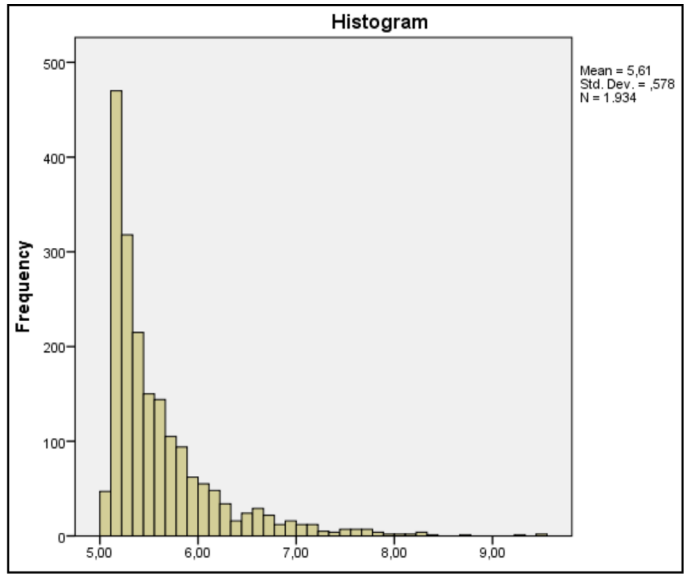

Figure 2. Distribution of serum potassium values of patients
Std. Dev.: Standard deviation

Table 2. AKI, hemodialysis, CKD, hospitalization, intensive care admission and gender comparisons of patients with hyperkalemia who died within 7 days

		7-day mortality in the hyperpotassemia group				
		Death		Survival		p value
		n	%	n	%	
AKI		64	21.5	233	78.5	<0.001
Hemodialysis		36	16.5	182	83.5	<0.001
CKD		23	6.0	363	94.0	0.503
Hospital admission		89	10.9	731	89.1	<0.001
ICU admission		73	32.0	155	68.0	<0.001
Gender	Male	62	7.2	801	92.8	0.466
	Female	68	6.3	1003	93.7	

AKI: Acute kidney injury, CKD: Chronic kidney disease, ICU: Intensive care unit

It was seen that 89 (68.4%) of 130 patients who died within a week were hospitalized (10.9% of 820 hospitalized patients). It was found that 3.7% of the patients who were not hospitalized (41 patients) died within seven days. The frequency of hospitalization in patients with hyperpotassemia who died within a week was statistically significant, which was higher than those who did not die (p<0.001).

It was observed that 73 of 130 patients (56.1%) who died within a week were treated by hospitalization in intensive care (32.0% of 228 patients hospitalized in intensive care). It was found that 3.3% (57 patients) of the patients who were not hospitalized in intensive care died within seven days. Patients with hyperkalemia who died within a week were more frequently hospitalized in intensive care than those who did not die (p<0.001).

When the gender analysis of 130 patients who died in a week was done, it was seen that 62 female patients (7.2% of female patients), 68 male patients (6.3% of male patients) died within seven days, and there was no statistical difference between sexes in terms of death within seven days (p=0.466).

When 245 patients who died within 28 days in patients with hyperpotassemia were examined (Table 3), it was seen that patients with AKI compared to those who were not (p<0.001), patients who received hemodialysis compared to those who did not (p<0.001), patients who were hospitalized due to the indication for hospitalization (p<0.001), and patients who were admitted to the ICU due to the ICU indication compared to those who were not (p<0.001) died within 28 days in a greater ratio, which was statistically significant. In the patient group, it was found that there was no statistically significant difference (p=0.818) in the 28 days mortality rate of female patients with hyperkalemia compared to male patients.

Although there was no difference between patients with CKD and patients without CKD in 7-day deaths, when the 28-day deaths of patients with hyperkalemia were evaluated, it was observed that patients without CKD died more than patients with CKD, which was statistically significant (p=0.042). It was concluded that the reason for this was the fact that there were AKI patients with a high mortality rate among patients without CKD (These patients were removed from the CKD group and included in the AKI group). For this reason, AKI patients were excluded from the study group and an additional statistical analysis was performed for CKD patients. We found that if AKI patients among patients without CKD were excluded, the 7-day and 28-day rate of CKD patients might be higher than those without CKD.

In the statistical analysis performed when AKI patients were excluded (1638 patients), the 1-week mortality rate was found to be significantly higher in patients with CKD (p=0.027). Although the 28-day mortality rate was high in patients with CKD, no statistically significant difference was found (p=0.188) (Table 4).

The rate of hospitalization and hemodialysis in hyperkalemia patients with AKI was found to be significantly higher than those without AKI (p<0.001).

In the ROC analysis performed on samples with hyperpotassemia, a relationship was observed between potassium values and 7 and 28-day mortality (p<0.001 AUC=0.762, p<0.001 AUC=0.696). However, it was determined that mortality was found even with potassium values close to normal (Figure 3).

When 460 patients with hyperkalemia who died within 1 year were examined, the median of potassium samples was 5.65 mEq/L (IQR25: 5.28-IQR75: 6.16). In addition, it was observed that almost 70% of hyperkalemia patients who died within a year had potassium values lower than 6 mEq/L. Significant mortality was observed in patients close to normal potassium levels.

Table 3. AKI, hemodialysis, CKD, hospitalization, intensive care admission and gender comparisons of patients with hyperpotassemia who died within 28 days

		28-day mortality in hyperpotassemia group				
		Death		Survival		p value
		N	%	N	%	
AKI		114	38.4	183	61.6	<0.001
Hemodialysis		68	31.2	150	68.8	<0.001
CKD		37	9.6	349	90.4	0.042
Hospital admission		186	22.7	634	77.3	<0.001
ICU admission		120	52.6	108	47.4	<0.001
Gender	Female	111	12.9	752	87.1	0.818
	Male	134	12.5	937	87.5	

AKI: Acute kidney injury, CKD: Chronic kidney disease, ICU: Intensive care unit

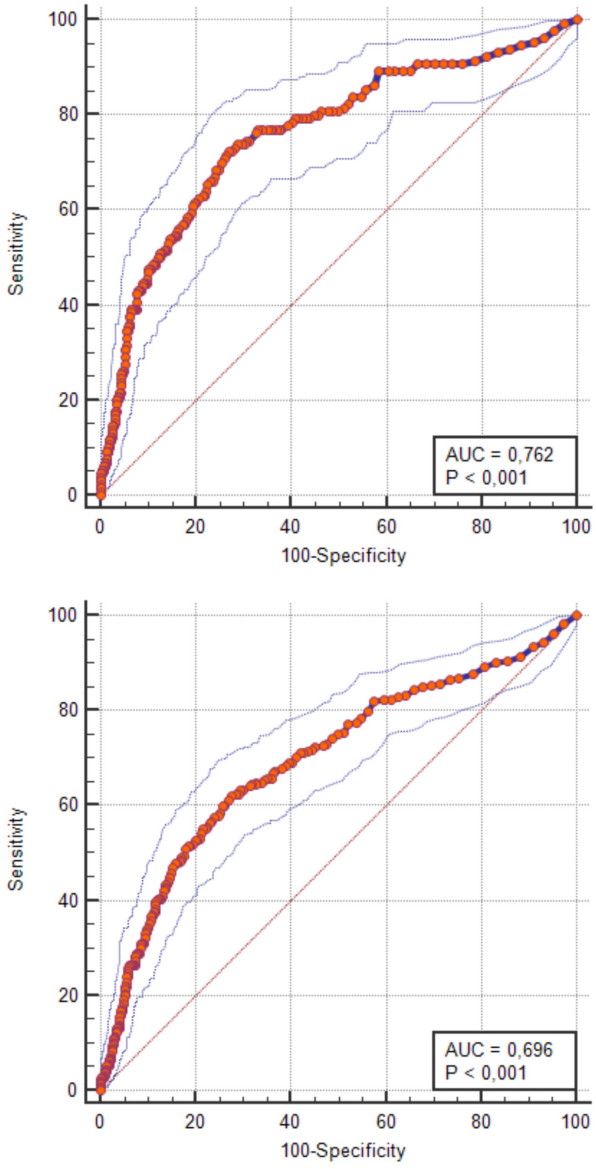

Figure 3. ROC analysis performed on samples with hyperpotassemia, a relationship was observed between potassium values and 7 and 28-day mortality

ROC: Receiver operating characteristics, AUC: Area under the curve

Table 4. 7-day and 28-day mortality of CKD patients when AKI patients are removed

	AKI patients excluded, (n=1,638)				
	Death		Survival		p value
	n	%	n	%	
7-day mortality	23	6.0	363	94.0	0.027
28-day mortality	37	9.6	349	90.4	0.188

CKD: Chronic kidney disease, AKI: Acute kidney injury, n: Number

As a result, it was found that the frequency of AKI, hemodialysis, hospitalization and intensive care admission was higher in all patient groups who died in 7 days and 28 days in patients with hyperpotassemia and were statistically significant (Table 5). There was no statistical increase in 7-day and 28-day mortality in CKD patients without AKI.

Discussion

In our study, false potassium abnormality was detected in 532 (19.5%) (2.8% of all samples) measurement patients. In the study conducted by Singer et al. (11), false potassium abnormality was detected in 3.6% and the samples showing this abnormality were excluded. This result is also consistent with our study.

In our study, the gender distribution was 48.5% (1,502 patients) female and 51.5% (1,589 patients) male. In the study by Singler et al. (12), the gender distribution was found to be 54% female and 46% male. In our study, the mean age of patients with hyperkalemia was 61.6 (SD: 18.94). In the study conducted at Hacettepe University Hospital, the average age of hyperpotassemia patients was found to be 56.8 (SD: 17) (12). In a study conducted in the USA, the average age of all patients included in the study was found to be 49 (SD: 22) (11). It was observed that patients with hyperkalemia in the population in our study were older compared to other studies.

In our study, the median potassium level of hyperkalemia patients was 5.40 mEq/L (IQR: 0.56). In the study conducted in South Korea by An et al. (13), the mean serum potassium level of patients with hyperkalemia was found to be 5.7 mEq/L (SD: 1.5). Since there was no normal distribution in the distribution of potassium levels in our study, the median was used, and since in the study we compared our findings, the average value was used, sufficient comparison could not be made.

While AKI was detected in 297 (15.4%) patients with hyperkalemia, and CKD was found in 386 (20.0%) of the patients who were hospitalized in Hacettepe University Hospital, 27% renal dysfunction was reported, although no distinction was made between acute and chronic (12).

It has been reported that hemodialysis was performed in 218 (11.3%) of hyperkalemia patients, while hemodialysis was performed in 7.9% of the patients hospitalized in Hacettepe University Hospital (12). In our study, it was found that the frequency of hemodialysis was higher. It is thought that this difference may be related to the tendency of nephrologists working in related hospitals to perform early or late hemodialysis.

It was found that the frequency of AKI, hemodialysis, hospitalization and intensive care hospitalization was higher

Table 5. Comparison of hospitalization and hemodialysis rates in patients with and without AKI and with and without CKD with hyperpotassemia

	Hospital admission				p value	Hemodialysis				p value
	Yes		No			Yes		No		
	n	%	n	%		n	%	n	%	
AKI	254	85.5	43	14.5	<0.001	90	30.3	207	69.7	<0.001
CKD	167	43.3	219	56.7	0.427	124	32.1	262	67.9	<0.001

AKI: Acute kidney injury, CKD: Chronic kidney disease, n: Number

in all patient groups who had hyperkalemia and died within 7 days and 28 days, which was statistically significant. It was observed that there was no statistically significant difference between patients with CKD and those who did not die within 7 days and patients who died within 7 days. It was found that it was statistically significant that patients without CKD died within 28 days more than those with CKD. It was concluded that the reason for this was AKI patients with a high mortality rate among patients without CKD.

Conclusion

In this study, it was found that AKI patients with hyperkalemia were associated with increased hospitalization, intensive care hospitalization, hemodialysis and death, and mortality could be seen in patients with hyperpotassemia close to normal values. Therefore, we think that all patients with increased potassium should be followed up closely, especially if AKI developed.

Ethics

Ethics Committee Approval: This study was approved by Akdeniz University Ethics Committee [no: 2012-KAEK (490), date: 09.08.2017].

Informed Consent: Retrospective study.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and/or Medical Practices: R.Y., O.E., Concept: R.Y., O.E., Design: R.Y., E.G., O.E., Data Collection and/or Processing: R.Y., E.G., O.E., Analysis and/or Interpretation: R.Y., E.G., O.E., Literature Search: R.Y., E.G., O.E., Writing: R.Y., E.G., O.E.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Bellomo R, Kellum JA, Ronco C. Acute kidney injury. Lancet. 2012;380:756-66.
2. Andreoli and Carpenter's Cecil Essentials of Medicine. 9th edition. 2015.
3. Rastergar A, Soleimani M. Hypokalaemia and hyperkalaemia. Postgrad Med J. 2001;77:759-64.
4. Schaefer TJ, Wolford RW. Disorders of potassium. Emerg Med Clin North Am. 2005;23:723-47.
5. Teh MM, Zaman MJS, Brooks AP, Li Voon Chong JSV. When is a high potassium not a high potassium? J R Soc Med. 2003;96:354-5.
6. Tran HA. Extreme hyperkalemia. South Med J. 2005;98:729-32.
7. Ahee P, Crowe AV. The management of hyperkalaemia in the emergency department. J Accid Emerg Med. 2000;17:188-91.
8. Gilligan S, Raphael KL. Hyperkalemia and Hypokalemia in CKD: Prevalence, Risk Factors, and Clinical Outcomes. Adv Chronic Kidney Dis. 2017;24:315-8.
9. Montford JR, Linas S. How dangerous is hyperkalemia? J Am Soc Nephrol. 2017;28:3155-65.
10. Nilsson E, Gasparini A, Ärnlöv J, Xu H, Henriksson KM, Coresh J, et al. Incidence and determinants of hyperkalemia and hypokalemia in a large healthcare system. Int J Cardiol. 2017;245:277-84.
11. Singer AJ, Thode Jr HC, Peacock WF. A retrospective study of emergency department potassium disturbances: severity, treatment, and outcomes. Clin Exp Emerg Med. 2017;4:73-9.
12. Eliacik E, Yildirim T, Sahin U, Kizilarslanoglu C, Tapan U, Aybal-Kutlugun A, et al. Potassium abnormalities in current clinical practice: Frequency, causes, severity and management. Med Princ Pract. 2015;24:271-5.
13. An JN, Lee JP, Jeon HJ, Kim DH, Oh YK, Kim YS, et al. Severe hyperkalemia requiring hospitalization: Predictors of mortality. Crit Care. 2012;16:R225.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.93653
Eurasian J Emerg Med. 2022;21(2): 106-13

How Can We Detect Delirium Easier Among Oncologic Patients in the Emergency Department?

Mustafa Boz, Nalan Metin Aksu, Elif Öztürk, Mehmet Mahir Kunt, Ali Batur

Department of Emergency Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey

Abstract

Aim: The study was planned to assess delirium for the oncologic patients admitted to ED with the complaint of altered level of consciousness, based on Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) diagnostic criteria, research for influencing etiologic factors and comparison of the brief Confusion Rating Method (bCAM), Mini Mental State Examination (MMSE) and New Delirium Rating Scale (NDRS), which are considered as delirium screening tests.

Materials and Methods: The Richmond Agitation-Sedation Scales (RASS) calculated for all patients before applying bCAM. The patients with the RASS score between -3 and +4 had been evaluated with bCAM. Delirium was diagnosed when the third or fourth characteristic was positive as well as the first two. The MMSE and NDRS scores of all patients and the duration of three tests were calculated.

Results: The MMSE and NDRS scores were 13.46±3.78 (7-20) and 21.42±3.28 (11-26) in the patients who were in delirium, respectively. Harmony between bCAM and MMSE are also statistically significant (Eta=0.70). Application period of bCAM was the shortest as 46.92±6.16 (30-60) sec.

Conclusion: bCAM was applied in the shortest period of time. This result is very useful for the EDs which are racing against time in the world.

Keywords: Delirium, cancer, bCAM, NDRS, emergency department

Introduction

Among cancer patients' cognitive problems are the most frequently reported symptoms during treatment, especially related to chemotherapy (1), and with a prevalence of delirium occurring in as many as 88% of patients with advanced cancer (2). As delirium impairs recognition of physical symptoms, it complicates achieving optimal symptom management, especially pain control in the emergency department (ED). Furthermore, delirium in patients with cancer is associated with significantly longer hospital stays, greater and longer functional decline, shorter life expectancy and a greater risk of death during acute treatment (3).

A diagnosis in the ED could help to optimize therapeutic approaches and improve clinical outcomes and potentially lower health care costs. Despite its importance of early recognition and treatment, the frequency of delirium among patients with cancer presenting to the emergency department is still unknown and often missed or misdiagnosed as worsening pain, depression, or anxiety (4).

Due to dynamic environment prolonged assessments for delirium are not appropriate in the ED settings and brief and sensitive tools are needed. As a tertiary care, academic ED, cancer patients visiting our emergency department have higher rates and longer lengths of stay in ED.

The Mini Mental State Examination, the brief Confusion Assessment Method (bCAM), and the New Delirium Rating Scale (NDRS) are used for quantitative measurement of cognitive status in adults.

Therefore, in this study we intend to assess delirium for the patients admitted to ED with the complaint of altered level of consciousness with a known malignancy, based on Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)

Corresponding Author: Prof. Nalan Metin Aksu, M.D., Department of Emergency Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey
E-mail: nametaksu@yahoo.com.tr ORCID ID: orcid.org/0000-0003-2256-5187

Received: 28.05.2021
Accepted: 02.09.2021

Cite this article as: Boz M, Metin Aksu N, Öztürk E, Kunt MM, Batur A. How Can We Detect Delirium Easier Among Oncologic Patients in the Emergency Department? Eurasian J Emerg Med. 2022;21(2):106-13.

diagnostic criteria, research for influencing etiologic factors and comparison of the bCAM, MMSE and NDRS, which are considered as delirium screening tests.

Materials and Methods

This was a prospective observational study. Local institutional Ethics Committee approval was obtained from Hacettepe University in October 2015 (GO 15/655-23). Written informed consent was obtained from all participants.

This study was set up between November 15, 2015 and May 31, 2016. The patients over 18 years of age who admitted to ED with the complaint of altered level of consciousness with a known malignancy were included in the study. Patients who left the ED without permission, those who refused, or were unable to participate were excluded from the study.

For each patient; age, gender, duration of consciousness blurring, existing malignancy, whether the patient had a similar complaint earlier, if so, how long ago it took place, previous diagnosis, consultations, outcome, Glasgow Coma Scale (GCS) were recorded.

If the patients had the complaint of altered level of consciousness previously, this situation has been separated to 0-1 month, 1-6 months or >6 months' sections. The diagnoses have been grouped as; neurological, infectious, cardiopulmonary diseases, metabolic or electrolyte disorder, trauma, drug induced, psychiatric and other diseases. The outcome of the patients stated as; discharged/exitus in ED, discharged/exitus in the ward, discharged/exitus in intensive care unit (ICU).

RASS calculated for all of the patients before applying the bCAM. Delirium evaluation could not be made when the RASS score was -4 or -5. In pursuance of reference diagnosis, we determined according to the fourth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). The patients with the RASS score between -3 and +4 were evaluated with the bCAM, MMSE and NDRS. The scores and the duration of each tests were calculated.

bCAM has 4 features: Altered mental status, or fluctuating course, inattention, altered level of consciousness and disorganized thinking (Figure 1) (5). Delirium was diagnosed due to the bCAM when both features 1 and 2 were present and either features 3 or 4 was present. MMSE can be implemented in a short time and its validity has been proven. It assesses orientation, recall, retention, and language ability. The NRDS which was developed by Ok et al. (6) for intensive care settings, evaluates the cardinal features of delirium, such as acute or fluctuating onset, inattention, disorganized thinking and altered level of consciousness. It is a 10-item, observer-rated scale based both on DSM-IV and on symptoms drawn from previous clinical research (Figure 2). Study protocol is given in the Figure 3.

Statistical Analysis

SPSS for Windows version 20 program (IBM Corp., Armonk, NY, USA) was used for the statistical analysis of the findings obtained in the study. Numerical variables were shown with average ± standard deviation or median (minimum-maximum); attribute variables were shown in numbers and percentages. The difference between the groups in terms of attribute variables was investigated by chi-square test. In case of occurrence whether there is a difference or not in numerical variables between the two groups depending on the parametric test assumptions evaluated according to t-test in independent groups, and in the other case according to Mann-Whitney U test. The significance level was determined as $p<0.05$.

Results

Totally 195 patients were included; 112 (57.4%) were male and 83 (42.6%) were female. The average age of these patients was 69 (25-92).

The present malignancies of the patients are shown in Figure 4. The most common malignant disease was lung neoplasm in 60 patients (30.8%). The most common diagnosis was pneumonia in 85 patients (43.6%).

According to the DSM-IV diagnostic criteria and results of bCAM, MMSE and NDRS tests, delirium was diagnosed in 26 of 195 patients (13.3%), no delirium was detected in 117 patients (60%), and no test could be made to 52 patients (26.7%) with RASS -4 or -5.

No statistically significant difference was found according to gender as 13 (50%) of the 26 patients with delirium were female and 13 (50%) of them were male ($p=0.353$). No statistically significant difference was found according to age as the average age of the 26 patients with delirium was 68.04±12.49, and 117 patients without delirium were 66.53±11.38 ($p=0.548$) (Table 1).

We found that the presence of accompanying illness increased the risk of delirium and 100% of patients with delirium were found to have an accompanying disease rather than a malignancy (Table 2). Among 26 patients with delirium nine patients (34.5%) were accomponied by acute infection (pneumonia, urinary tract infection and typhlitis), seven (26.9%) hepatic encephalopathy, five (19.2%) new diagnosis of intracranial mass and five (19.2%) hyponatremia diagnosis.

The mean of MMSE and NDRS scores of 26 patients with delirium was 13.46±3.78 (7-20), 21.42±3.28 (11-26) respectively; while 117 patients without delirium had a mean of MMSE scores 22.43±3.49 (6-27), and a mean of NDRS scores 8.53±0.74 (6-10). Statistically, strong positive correlation of total scores between the tests was found between bCAM and NDRS (Eta=0.95). Correlation between bCAM and MMSE was also statistically significant (Eta=0.70). Although less than the other two, correlation between MMSE and NDRS was also statistically significant (Eta=0.44). bCAM was performed in the shortest time of period among the other test, with an application period of was measured as 46.92±6.16 (30-60) seconds.Whereas the mean of application period of MMSE and NDRSA was measured as 256.89±24.31 (200-320) and 273.79±25.48 (230-360) seconds respectively (Table 2).

Discussion

In a study by Sharma et al. (7); they expressed that the incidence of delirium was reported in a wide range from 11% to 87% in studies, such as the type of patient population, the type of study, and the use of various diagnostic scales. In our study, delirium incidence was found to be 13.3%. This result is consistent with many studies.

In our study, delirium screening tests were applied immediately after the ED admission. In a study by Ely et al. (8); it has been reported that the delirium starts on average between the second and the third day after having settled in the intensive care unit and lasts for an average of 3-4 days although it can last up to 60 days. In our study, patients were assessed for delirium once on all tests within the same day. This probably reduced our rate of delirium in our ED.

In a study of Ely et al. (9) in which they were investigating sociodemographic characteristics of delirium; they expressed that aging is one of the factors that increase the tendency to delirium. In a recent study conducted in an emergency department, Brich et al. (10) found that female sex was slightly higher as 53.7%. There was no statistically significant difference according to sex and mean age in our study. However, as the average age of the delirium group was higher, it is in line with other works done before.

In our study, 20 (77%) of patients with delirium were in terminal period of cancer. In a study held in an acute paliative care unit, delirium occurance rate in patients with advanced cancer found to be 42-45% on admission and for first onset after admission. Lawlor (11) reported that delirium prevalance in ptients with cancer in the ED settings was 9%. Uchida et al. (12) reported 43% insidence of delirium in advanced cance patients and 75% of the patients received a terminal prognosis.

In our study the most common subgroup was lung cancer similar to the Uchida et al. (12) study in which lung cancer (74%) was the most common one also.

Sharma et al. (7) expressed that smoking, presence of acidosis, higher APACHE-II scores and use of sedative medications were found to more frequently seen in the incidence delirium group comparing non delirius group. Breitbart et al. (13) stated that multiple etiologies (67.3%) were more common than single etiologies as the cause of delirium among hospitalized cancer patients and in their study the most common etiologies for delirium included opioid analgesics (58.4%), corticosteroids (27.7%), systemic infection (38.6%), hypoxia (25.7%). In our study we found that the presence of an accompanying illness increased the risk of delirium and all of the patients with delirium were found to have accompanying disease.

Many scales were developed for the evaluation of delirium. However, there are few current scales developed, especially for intensive care and emergency patients (9). In our study, the bCAM, MMSE and NDRS were studied on cancer patients

Table 1. Distribution of patients with and without delirium according to gender, age, and diagnosis

	With delirium (n=26)	Without delirium (n=117)	Total (n=143)
Gender			
Female	13 (50%)	44 (37.6%)	57 (39.8%)
Male	13 (50%)	73 (62.4%)	86 (60.2%)
Age (mean ± SD)	68.04±12.49	66.53±11.38	
Diagnosis			
Newly diagnosed intracranial mass	5 (19.2%)	4 (3.4%)	9 (6.3%)
Pneumonia	5 (19.2%)	58 (49.6%)	63 (44.1%)
Urinary tract infections	3 (11.5%)	13 (11.1%)	16 (11.2%)
Hyponatremia	5 (19.2%)	13 (11.1%)	18 (12.6%)
Ischemic cerebrovascular event	-	4 (3.4%)	4 (2.8%)
Generalized seizure	-	5 (4.3%)	5 (3, 5%)
Hepatic encephalopathy	7 (26.9%)	-	7 (4.9%)
Carbon dioxide retention	-	3 (2.6%)	3 (2.1%)
Hypoglycemia	-	1 (0.9%)	1 (0.7%)
Gastrointestinal bleeding	-	8 (%6.8)	8 (5.6%)
Cardiac tamponade	-	2 (1.7%)	2 (1.4%)
Diabetic ketoacidosis	-	2 (1.7%)	2 (1.4%)
Typhlitis	1 (3.8%)	4 (3.4%)	5 (3.5%)

SD: Standard deviation, n: Number of the patients

Table 2. MMT/NDRS scores and application period for the patients with and without delirium according to bCAM			
	With delirium	**Without delirium**	**Total**
Delirium acoording to bCAM (n)	26	117	143
Scores			
MMT	13.46±3.78	22.43±3.49	20.80±4.95
NDRS	21.42±3.28	8.53±0.74	10.87±5.22
Application period [seconds ± SD (min-max)]			
bCAM	46.92±6.16 (30-60)		
MMT	256.89±24.31 (200-320)		
NDRS	273.79±25.48 (230-360)		
bCAM: Brief confusion assesment method, MMT: Mini mental test, NDRS: New Delirium Rating Scale, SD: Standard deviation, min: Minimum, max: Maximum			

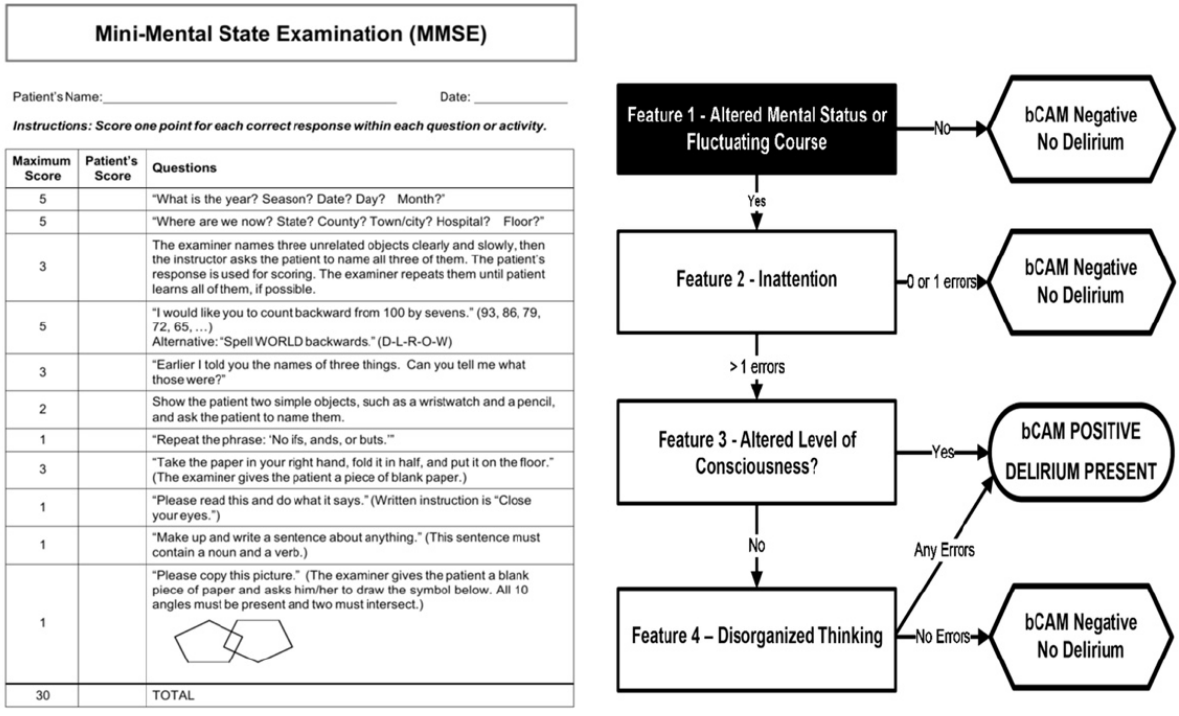

Figure 1. The Mini Mental State Examination (MMSE) and the brief the brief Confusion Assessment Method (bCAM)

who came to our ED with altered level of consciousness complaints.

The "Confirmation Assessment Method for the Intensive Care Unit (CAM-ICU)" was developed by Ely et al. (14) for use in intensive care units to detect delirium in ICU patients who cannot normally communicate due to mechanical ventilation. In this first study where they defined CAM-ICU, 38 patients in ICU were evaluated daily with CAM-ICU by two nurses and one ICU specialist and compared to DSM-IV criteria which is accepted as a reference test. Delirium was detected in 33 of the 38 patients (87%) in ICU, and it was concluded that CAM-ICU might be a useful tool for delirium detection when used by nurses and doctors in this difficult patient population (14). In another study, McNicoll et al. (15) have compared "Confirmation Assessment Method (CAM)" and CAM-ICU. Twenty-two patients aged 65 years or older who were admitted to ICU were included in the study. Two trained clinicians interviewed each patient for 10 minutes and evaluated the patients according to four key CAM criteria; acuteness, inattention, disorganized thinking, and altered level of consciousness. One researcher used CAM

New Delirium Rating Scale (NDRS)
1) Psychomotor activity
0. Normal
1. Mild increase (agitation or restlessness) or decrease (mild retardation) in acitivity
2. Moderate increase (intending to leave the ward, grasping the tubes, groping the bed) or decrease (performing activity on command) in activity
3. Excessive increase (exitation deserving fixation) or decrease (not even performing activity on command) in activity
2) Orientation
0. Normal
1. Disorientation for time, or place, or person
2. Disorientation for time and place, or time and person, or place and person
3. Disorientation for time, and place, and person (rate no answer due to confusion here)
3) Attention
0. Normal
1. Difficulty in concentration (maintaining his/her attention by himself/herself)
2. Moderate disturbance in attention, distractibility (maintaining his/her attention on command)
3. Total disturbance in attention (not even maintaining his/her attention on command)
4) Memmory
0. Normal
1. Disturbance in immediate or recent memory
2. Disturbance in immedite and rrecent memory
3. Disturbance in immediate or recent memory (rate no answer due to confusion)
5) Perception
0. Normal
1. Vivid dreams and/or nightmares
2. Transient illusions and/or hallucinations
3. Definite illusions and/or hallucinations (hallucinatory experience)
6) Thinking
0. Normal
1. Partially disrupted thinking
2. Totally disrupted thinking
3. Incoherence
7) Thought content
0. Normal
1. Overvalued thought (does not act consistently and knows that is false)
2. Drafts of delusion (sometimes acts consistently and can inquire that it is false)
3. Delusion (acts consistently and cannot inquire that is false) or delusional experience
8) Sleep-wake cycle
0. Normal
1. Marked drowsiness daytime while being awake most of the night
2. Sleeping daytime while being awake all of the night
3. Almost not sleeping or always sleeping during both the day and the night
9) Diurnal variation
0. No fluctuation
1. Occurance of symptoms during the night while normal during the day
2. Occurance of symptoms continuously during the night and interruptedly during the day
3. Occurance of symptoms both during the day and the night fluctuatingly
10) Lability of mood
0. No fluctuation
1. Alternation or change in mood over the course of hours
2. Alternation or change in mood over the course of minutes (mood changes which are inappropiate to situation, including fear, anger or tearfulness)
3. Severse disinhibation of emotions (temper outbursts, uncontrolled laughter or crying)

Figure 2. The New Delirium Rating Score (NDRS)

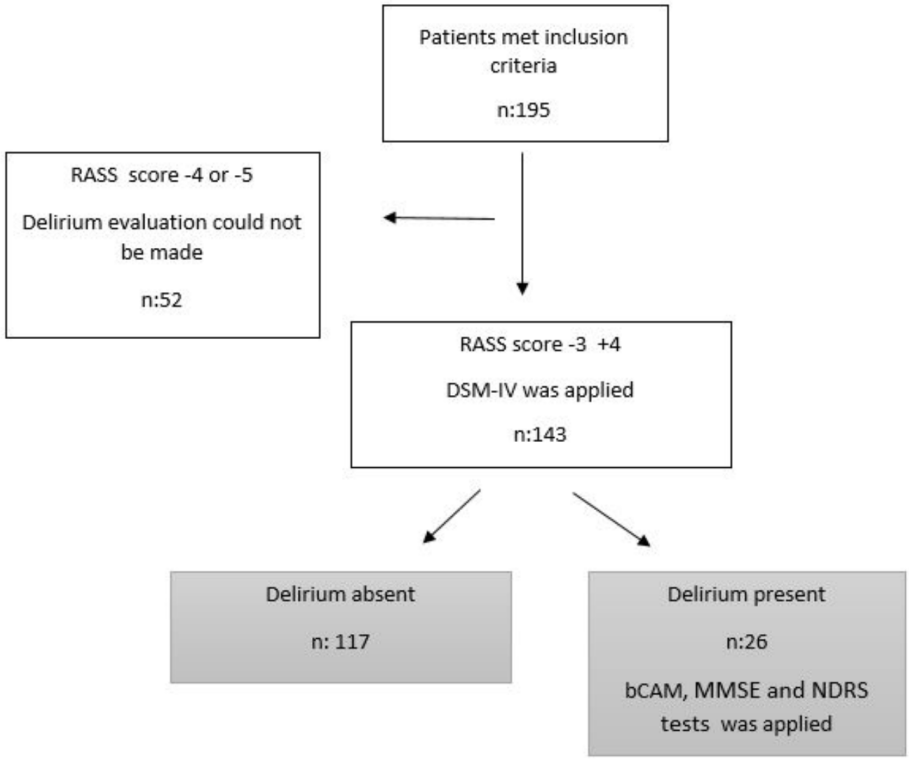

Figure 3. Study protocol

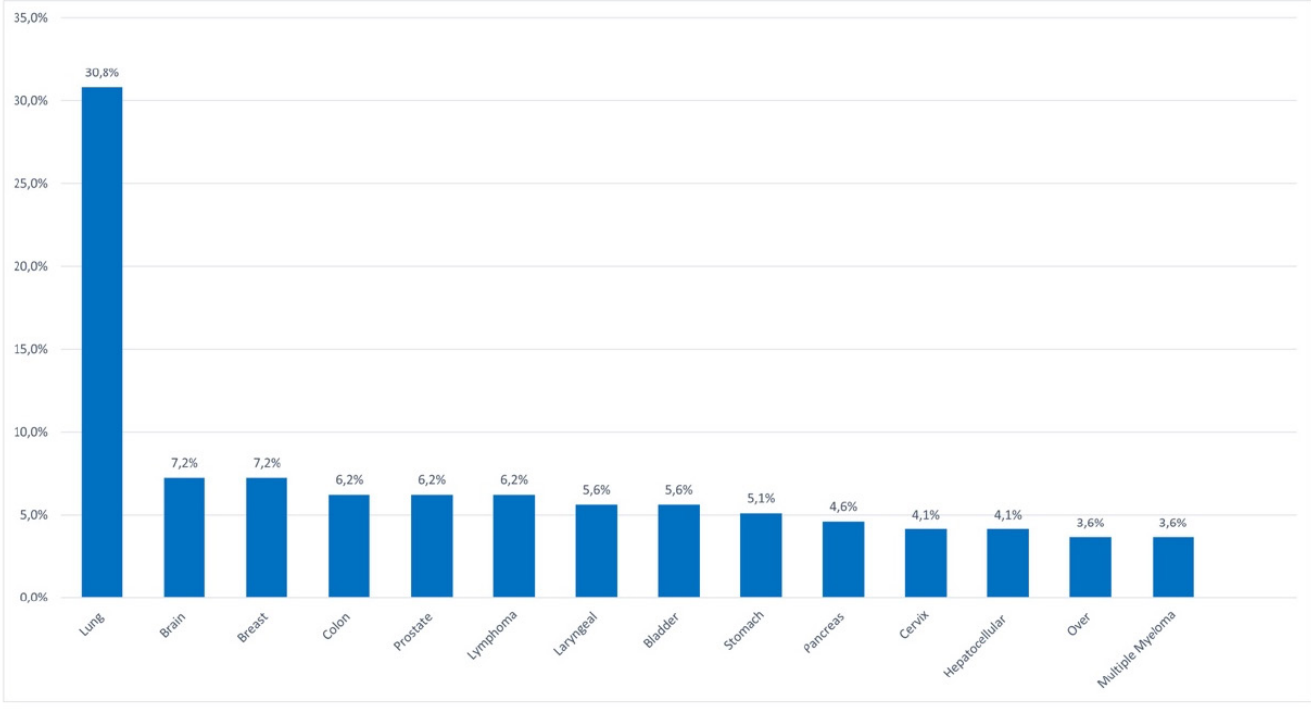

Figure 4. Distribution of the patients according to existing malignancies

method with "Mini Mental State Examination", while the other researcher used CAM-ICU. The delirium rate was 68% according to CAM, and 50% according to CAM-ICU. When two methods were compared, compliance was 82%. The differences in conclusions were accepted to be because of the fact that CAM was a more detailed cognitive test. Because of the easy application method and short-term implementation of CAM, it was concluded to be applied to ICU patients and can be used to detect latent delirium cases in intensive care patients who are able to speak and non-intubated.

In our study, the correspondence between bCAM and MMSE was statistically significant. This result is consistent with other studies and shows that the MMSE score is lower in patients with delirium.

Ok et al. (6) developed NDRS as a result of the study in the ICU in Turkey in 2010. Delirium was diagnosed in three patients (10%) among 30 patients who were treated in the ICU for longer than 24 hours without endotracheal intubation. They admitted the cut off value for delirium diagnosis as 11. In our study, the correspondence between bCAM and NDRS was statistically significant; the mean NDRS score in the patients with delirium was higher than the patients without delirium. This result is consistent with other studies and shows that the NDRS score is higher in patients with delirium.

Baten et al. (16) applied bCAM in the emergency settings during the daily work routine by emergency physicians rather than a neurologist/psychiatrist and found that bCAM took a median time of 3 minutes to perform, which is longer than our study as well as the literature and they speculated that duration of the test will be shorter when bCAM is routinely performed. When we compare the duration of the tests made in emergency service, the bCAM was shorter than MMSE and NDRS.

Although cancer patients were admitted to our ED more than surgical or medical emergencies apart from oncologic emergencies the number of the patients included in the study was fewer than expected. This was the limitation of this study.

Conclusion

bCAM is easier to apply to detect delirium in ED and it is more suitable for the ED patients because of its short application period. This result is very valuable to us as the EDs are units racing against time in our country and in the world.

Ethics

Ethics Committee Approval: This prospective study was approved by Hacettepe University Institutional Ethics Committee in October 2015 (GO 15/655-23).

Informed Consent: Written informed consents were obtained from study participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.B., N.M.A., Design: M.B., N.M.A., M.M.K., Data Collection and/or Processing: M.B., E.Ö., M.M.K., A.B., Analysis and/or Interpretation: M.B., E.Ö., A.B., Literature Search: M.B., N.M.A., E.Ö., M.M.K., A.B., Writing: M.B., N.M.A., E.Ö., M.M.K., A.B.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Janelsins MC, Kesler SR, Ahles TA, Morrow GR. Prevalence, mechanisms, and management of cancer-related cognitive impairment. Int Rev Psychiatry. 2014;26:102-13.
2. Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, Suarez-Almazor ME, et al. Occurrence, Causes, and Outcome of Delirium in Patients With Advanced Cancer. Arch Intern Med. 2000;160:786-94.
3. Schuurmans MJ, Duursma SA, Shortridge-Baggett LM. Early recognition of delirium: Review of the literature. J Clin Nurs. 2001. doi:10.1111/j.1365-2702.2001.00548.x
4. Elsayem AF, Bruera E, Valentine AD, Warneke CL, Yeung SCJ, Page VD, et al. Delirium frequency among advanced cancer patients presenting to an emergency department: A prospective, randomized, observational study. Cancer. 2016;122:2918-24.
5. Inouye SK, Van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: The confusion assessment method: A new method for detection of delirium. Ann Intern Med. 1990;113:941-8.
6. Ok G, Tok D, Erbüyün K, Turan E, Aydemir Ö. New delirium rating scale for ICU. Noropsikiyatri Ars. 2010;47:36-9.
7. Sharma A, Malhotra S, Grover S, Jindal SK. Incidence, prevalence, risk factor and outcome of delirium in intensive care unit: A study from India. Gen Hosp Psychiatry. 2012;34:639-46.
8. Ely E, Gautam S, Margolin R, Francis J, May L, Speroff T, et al. The impact of delirium in the intensive care unit on hospital length of stay. Intensive Care Med. 2001;27:1892-900.
9. Ely EW, Bernard GR, Speroff T, et al. Delirium in mechanically ventilated patients: Validity and reliability of the Confusion Assessment Method for the intensive care unit (CAM-ICU). J Am Med Assoc. 2001;286:2703-10.
10. Brich J, Baten V, Wußmann J, Heupel-Reuter M, Perlov E, Klöppel S, et al. Detecting delirium in elderly medical emergency patients: validation and subsequent modification of the German Nursing Delirium Screening Scale. Intern Emerg Med. 2019;14:767-76.
11. Lawlor PG. Cancer patients with delirium in the emergency department: A frequent and distressing problem that calls for better assessment. Cancer. 2016;122:2783-6.
12. Uchida M, Okuyama T, Ito Y, Nakaguchi T, Miyazaki M, Sakamoto M, et al. Prevalence, course and factors associated with delirium in elderly patients with advanced cancer: a longitudinal observational study. Jpn J Clin Oncol. 2015;45:934-40.
13. Breitbart W, Gibson C, Tremblay A. The delirium experience: delirium recall and delirium-related distress in hospitalized patients with cancer, their spouses/caregivers, and their nurses. Psychosomatics. 2002;43:183-94.

14. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: Validation of the Confusion Assessment Method for the intensive care unit (CAM-ICU). Crit Care Med. 2001;29:1370-9.

15. McNicoll L, Pisani MA, Ely EW, Gifford D, Inouye SK. Detection of delirium in the intensive care unit: Comparison of confusion assessment method for the intensive care unit with confusion assessment method ratings. J Am Geriatr Soc. 2005;53:495-500.

16. Baten V, Busch H, Busche C, Schmid B, Heupel-Reuter M, Perlov E, et al. Validation of the Brief Confusion Assessment Method for Screening Delirium in Elderly Medical Patients in a German Emergency Department. Acad Emerg Med. 2018;25:1251-62.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.86658
Eurasian J Emerg Med. 2022;21(2): 114-9

Analysis of the Degree of Accuracy and Reliability of Emergency Medicine Residents in Interpreting Computed Tomography of the Abdomen

Sümeyye Tuğba Sarkı Cander[1], Şule Akköse Aydın[1], Vahide Aslıhan Durak[1], Murat Çetin[2], Deniz Sığırlı[3]

[1]Department of Emergency Medicine, Bursa Uludağ University Faculty of Medicine, Bursa, Turkey
[2]Department of First Aid and Emergency Medicine, İzmir Tınaztepe University Faculty of Medicine, İzmir, Turkey
[3]Department of Biostatistics, Bursa Uludağ University Faculty of Medicine, Bursa, Turkey

Abstract

Aim: In this study, we aimed to investigate the accuracy and reliability of emergency medicine residents in the interpretation of radiological investigation of patients with trauma, who received abdominal computed tomography in the emergency department.

Materials and Methods: We prospectively evaluated the reports of 200 patients who presented to the emergency medicine department of a university hospital with trauma, and who received abdominal computed tomography (CT) due to suspected abdominal pathology.

Results: In this study, 33% (66/200) of the patients were female and 67% (134/200) were male. CT scans of these 200 patients were examined by emergency medicine residents and radiology specialists. The results of the study showed that emergency medicine residents performed well in interpreting abdominal CT scans of patients with trauma with an agreement rate of 90.5%. Evaluation of the results obtained in our study suggested that emergency medicine residents generally performed well in interpreting abdominal CT scans of patients with trauma with suspected abdominal pathology in the emergency room.

Conclusion: The high rate of agreement may be associated with the fact that emergency medicine residents are usually the first physicians who meet and treat patients with trauma and thus have gained sufficient experience in this field.

Keywords: Abdominal trauma, computed tomography, emergency department, emergency resident

Introduction

While the extent and workload of emergency services increase every single day, the choice for easily accessible and effective examinations becomes very important in-patient management. It is observed that laboratory tests and imaging performed in the emergency department account for more than 40% of the total cost (1).

More than 11 million people die every year in the world and approximately 8% of the total deaths are due to trauma. The mortality rates of patients with abdominal trauma varied between 12.6% and 21.3%, where the spleen and liver were reportedly the most frequently injured organs (2).

Computed tomography (CT) has emerged as the main imaging method for evaluating patients with multiple trauma subsequent to the introduction of multi-slice computed tomography (MSCT) (3). MSCT has been incorporated in the current trauma imaging protocol because of its widespread accessibility and adoption (3). In major intraabdominal injuries, the sensitivity and specificity of MSCT are 97-98% and 97-99%, respectively (4).

Although interpretation of abdominal CT is a critical issue during emergencies, there are limited number of studies that have analyzed the reliability and accuracy of interpretations of abdominal CT images performed by emergency medicine residents (EMRs). The purpose of our study is to investigate the accuracy and reliability of EMRs with respect to interpretation of

Corresponding Author: Assoc. Prof. Vahide Aslıhan Durak, M.D., Department of Emergency Medicine, Bursa Uludağ University Faculty of Medicine, Bursa, Turkey
E-mail: aslidurakis@hotmail.com ORCID ID: orcid.org/0000-0003-0836-7862

Received: 12.06.2021
Accepted: 17.09.2021

Cite this article as: Sarkı Cander ST, Akköse Aydın Ş, Durak VA, Çetin M, Sığırlı D. Analysis of the Degree of Accuracy and Reliability of Emergency Medicine Residents in Interpreting Computed Tomography of the Abdomen. Eurasian J Emerg Med. 2022;21(2):114-9.

CT scans of patients with trauma, who underwent abdominal CT in the emergency room.

Materials and Methods

This study was approved by the Clinical Research Ethics Committee of Bursa Uludağ University Faculty of Medicine, dated March 25, 2019 with approval number 2019-6/8. In this study, we included patients with trauma, above 18 years of age, who presented to the emergency department (ED) between April 4, 2019 and October 4, 2019 and who underwent abdominal CT due to suspected abdominal pathology. The focused assessment with sonography for trauma (FAST) scans of the patients were performed by the emergency medicine residents first and the patients who were with suspected abdomen pathologies and need further CT evaluation were included in this study. Also, the trauma patients who were under 18 years and pregnant were excluded from the study.

We compared the abdominal CT image interpretations performed by EMRs who had work experience of 2 years with the CT results that were edited and approved by radiologists. We evaluated CT images (coronal, axial, and sagittal sections) of the patients' abdomen using the Picture Archiving and Communication Systems from the monitors in the ED.

The presence of pathology in the examination was considered as "pathology exists". The findings of liver laceration, liver hematoma, splenic laceration, splenic hematoma, kidney injury, intraabdominal free fluid, intraabdominal free air, vascular injury, fracture in bone fragments were evaluated separately and recorded as "pathology exists" or "pathology does not exist."

We evaluated the consistency between the two interpretations by comparing the CT interpretation performed by EMRs with the official radiology report after the data recording process. While the results that either EMRs or radiologists evaluated as "pathology exists" and the other as "pathology does not exist" were considered inconsistent, the evaluations made by both the EMRs and radiologists as "pathology exists" or "pathology does not exist" were evaluated as consistent.

Statistical Analysis

We used the Shapiro-Wilk test for variables that were suitable for normal distribution. Variables that did not conform to normal distribution were given median (minimum-maximum) values. Categorical variables were given frequency and percentage values [n (%)]. McNemar test was used to evaluate the agreement between the determinations of the radiologist and the EMRs, and sensitivity, specificity, positive predictive value, and negative predictive value criteria were provided. IBM SPSS Statistics 23.0 (IBM Corp, Armonk, NY, USA) program was used for statistical analyses. Significance level was considered as α=0.05.

Results

During the six-month period, 33% of the patients who received abdominal CT due to suspected abdominal pathology were female and 67% were male. The median age of the traumatic cases was 40 (minimum-maximum: 19-92) years.

In the study, the most common cause of trauma mechanisms (37%) was the in-vehicle traffic accident. Other common causes of trauma mechanism were falls (32.5%) and motorcycle accident (12.0%). Table 1 shows the distribution of patients according to trauma mechanisms. While 50.5% of the patients with abdominal trauma who presented to the emergency service ended with discharge, there was no case of mortality (Table 1).

We reviewed the consistency between the interpretation of the abdominal CT reports performed by EMRs and radiologists. It was seen that two of the three patients with splenic hematoma (66.7%) reported by the radiologist as having pathology were evaluated by the EMR physicians as "pathology exists", whereas 193 (98%) of the 197 patients reported by the radiologist as having no pathology were evaluated as "pathology does not exist" by the EMRs. There was a significant agreement between the EMRs and radiologists in terms of splenic hematoma detection (p=0.375). Regarding splenic laceration, while the EMRs detected pathology in seven of the eight patients (87.5%) that the radiologist suggested pathology, EMRs considered "pathology does not exist" in 190 (99%) of the 192 patients that the radiologist reported no pathology. Therefore, there was a statistically significant agreement between radiologist and EMRs in detecting splenic laceration (p=1.000). There was a significant agreement between the interpretation performed by EMRs and radiologists with regards to liver hematoma (p=0.219), kidney injury (p=0.250), intraabdominal free fluid (p=0.057),

Table 1. Distribution of patients according to trauma mechanisms

Mechanism	**n**	**%**
Fall	65	32.5
In-vehicle traffic accident	74	37.0
Off-vehicle traffic accident	14	7.0
Motorcycle accident	24	12.0
Stab wounds	4	2.0
Blunt trauma	16	8.0
Tractor accident	3	1.5
Total	200	100

n: Number

intraabdominal free air (p=1.000), and fracture detection in bone fragments (p=1.000) when there was a meaningful fit. However, there was no significant agreement between the interpretations in terms of liver laceration (p=0.022). Regarding vascular injury, the p value could not be calculated, as there were no patients with positive pathology detection by EMR or radiologists. Among the 200 patients included in the study, there was no patient with pancreatic injury, and ureter and bladder injury (Table 2). In each subgroup, upon calculation of the sensitivity, specificity, positive predictive value, and negative predictive value criteria of evaluations performed by EMRs against the evaluations of radiologists, it was observed that the highest values were calculated for the determination of intraabdominal free air (Table 3).

In the present study, among all the patients presenting with abdominal trauma, the number of patients with at least one pathology as detected by the radiologists was 62, 54 of them were also detected by EMRs and the sensitivity of EMRs in detecting abdominal pathology was 87%. The number of patients with no pathology detected by radiologists was 138, and 127 of them were found to have no pathology by EMRs as well. The specificity of EMRs for abdominal pathology was 92%. There was a significant agreement between the CT comments made by the EMRs and the radiologists (p=0.648) (Table 4).

Discussion

Intervention and transfer to a hospital are of great significance for the survival of patients with trauma. In a study conducted by Pekdemir et al. (5) in 1997, 90.8% of the patients presented to the ED using a vehicle other than an ambulance. In the present study, it was noted that 28% (56) of the patients presented to the ED trauma unit as outpatients and 72% (144) were brought in by ambulance. In our study, the rate of admission using an ambulance is higher. This may be associated with the fact that trauma patients generally prefer ambulance service for hospital admission and that they are not well enough to present as outpatients following in/off-vehicle traffic accidents. The development of emergency health services has also led to an increase in the number of admissions via ambulance.

In our study, a review of trauma etiologies of the patients showed that the most frequent causes were the in/off-vehicle traffic

Table 2. Comparison of EMRs' and radiologists' interpretations of abdominal CT images by subgroups

EMR		Radiology		p value
		Pathology exists	Pathology does not exist	
Splenic hematoma	Pathology exists	2 (66.7)	4 (2.0)	0.375
	Pathology does not exist	1 (33.3)	193 (98.0)	
Splenic laceration	Pathology exists	7 (87.5)	2 (1.0)	1.000
	Pathology does not exist	1 (12.5)	190 (99.0)	
Liver hematoma	Pathology exists	6 (85.7)	5 (2.6)	0.219
	Pathology does not exist	1 (14.3)	188 (97.4)	
Liver laceration	Pathology exists	12 (85.7)	11 (5.9)	0.022
	Pathology does not exist	2 (14.3)	175 (94.1)	
Kidney injury	Pathology exists	2 (40.0)	0 (0.0)	0.250
	Pathology does not exist	3 (60.0)	195 (100.0)	
Intraabdominal free fluid	Pathology exists	2 (15.4)	3 (1.6)	0.057
	Pathology does not exist	11 (84.6)	184 (98.4)	
Intraabdominal free air	Pathology exists	1 (100.0)	0 (0.00)	1.000
	Pathology does not exist	0 (0.00)	199 (100.0)	
Fracture	Pathology exists	33 (97.1)	0 (0.00)	1.000
	Pathology does not exist	1 (2.9)	199 (100.0)	
Vascular injury	Pathology exists	0 (0.00)	-	-
	Pathology does not exist	0 (0.00)	-	

Data are provided as n (%) values. The p value is from the McNemar test.
EMR: Emergency medicine resident, CT: Computed tomography, n: Number

Table 3. Sensitivity, descriptiveness, PPD, and NPD criteria of EMRs in detecting abdominal pathologies				
Pathologies	**Sensitivity**	**Specificity**	**PPD**	**NPD**
Splenic hematoma	0.67	0.98	0.33	0.99
Splenic laceration	0.88	0.99	0.77	0.99
Liver hematoma	0.86	0.97	0.54	0.99
Liver laceration	0.86	0.94	0.52	0.98
Intraabdominal free fluid	0.15	0.98	0.40	0.94
Intraabdominal free air	1.00	1.00	1.00	1.00
Kidney injury	0.40	1.00	1.00	0.98
Fracture in bone fragments	0.97	1.00	1.00	0.99
PPD: Positive predictive value, NPD: Negative predictive value, EMR: Emergency medicine resident				

Table 4. Comparison of EMRs and radiologists by comparison of abdominal CT evaluations				
Consistency	**Radiologist**			**p value**
EMR	**Exists**	**Does not exist**	**Total**	
Exists	54 (87.1)	11 (8.0)	65 (32.5)	0.648
Does not exist	8 (12.9)	127 (92.0)	135 (67.5)	
Total	62	138	200 (100.0)	
Data are provided as n (%). EMR: Emergency medicine resident, CT: Computed tomography, n: Number				

accidents (44%) and falls (32%), whereas the least frequent cause was tractor accidents (1.5%). In a study conducted by Durdu et al. (6), the frequency of trauma etiologies was found as traffic accidents (58.6%), falling from height (14.9%), assault (11.9%), work accident (9.6%), stab wounds (4.8%), and firearm injuries (0.9%). In a study conducted by Bingol et al. (7), 61.4% of the patients presented following a traffic accident and 22.4% after a fall from height (7). In a study conducted by Champion et al. (8) on patients with multiple traumas, 49.1% of the admissions were due to traffic accidents, 16.5% due to fall from height, 10% due to gunshot wounds, and 9.5% due to stab wounds. In this respect, the results of our study are consistent with other studies in the literature.

In a study conducted by Gönültaş et al. (9), the mean age of patients who presented to the ED with abdominal trauma was 36.08±16.1 years, and 90 out of the total 113 patients were men. Further, 80 patients (70.8%) had blunt abdominal trauma, 28 patients (24.7%) had isolated liver, and two patients (1.7%) had splenic injury. In a study conducted by Makay et al. (10) on patients with abdominal trauma, 82.6% of the patients with a mean age of 33.4±12 years were male and 17.4% were female. It was observed that 50.7% of the patients were exposed to blunt trauma, whereas 49.3% had penetrating trauma. In patients with penetrating trauma, stab wounds were the most common (31.4%), whereas blunt trauma was most common due to traffic accidents (42%). In the present study, the number of patients exposed to blunt trauma was found to be much higher, whereas the number of patients exposed to penetrating trauma was less when compared with other studies. However, the number of male patients was higher among the patients admitted to the ED with abdominal trauma, as seen in other studies.

Studies investigating the consistency in radiographic interpretation between EMRs and radiologists are available in the literature. Bagheri-Hariri et al. (11) compared abdominopelvic CT interpretations performed by emergency physicians with radiology reports to evaluate the success of abdominopelvic CT interpretation of emergency physicians and found that emergency physicians were successful in interpreting abdominopelvic CT results ($p<0.0001$). A similar study conducted by Guven et al. (12), found the sensitivity of emergency physicians in detecting non-traumatic abdominal pathologies between 60-80%, while the specificity was found to be above 95%. In the present study, there was a statistically significant consistency between the interpretations of radiologists and EMRs with regards to interpretation of splenic hematoma ($p=0.375$), laceration ($p=1.000$), liver hematoma ($p=0.219$), detection of kidney injury ($p=0.250$), intraabdominal free fluid detection ($p=0.057$), intraabdominal free air detection ($p=1.000$), and

fracture detection in bone fragments (p=1.000). There was no statistically significant agreement between radiologists' and EMRs' detection of liver laceration (p=0.022). In our study, 90.5% agreement was found between the CT comments made by EMRs and radiologists in patients presenting with abdominal trauma (p=0.648). Accordingly, the sensitivity of EMRs in detecting pathologies in abdominal CT was found to be 87%, whereas the specificity was calculated as 92%.

According to the results of our study, we can conclude that there is no statistically significant agreement (p=0.022) between the interpretation of radiologists and EMRs regarding liver laceration. In the present study, 14 out of the total 200 patients had liver laceration according to the radiologists' final report, whereas 12 of them were considered as "pathology exists" by EMRs. One of the two patients, who was considered as "pathology does not exist" by EMRs was referred to intensive care, while the other patient was hospitalized in the relevant clinic. Since the patient admitted to the intensive care had splenic laceration, he underwent a splenectomy. The patient was transferred to the clinic after 5 days of intensive care hospitalization and was discharged after 2 days of clinical hospitalization. The other patient who was admitted to the relevant clinic did not develop any complications after clinical follow-up and was thus discharged. There was no report of adverse effect of mortality in the two patients whose pathology was not observed by EMRs.

In a study performed by Mucci et al. (13) investigated the consistency of EMR evaluations with expert radiologist reports in cranial CT results of 100 patients with trauma and suggested an 86.6% agreement between EMR evaluations and radiologist reports. Kang et al. (14) in their study investigated the accuracy of interpretations performed by EMRs and radiology residents' of abdominal CT images in patients with nontraumatic abdominal pain and found a consistency of 83.3% between the EMRs' evaluations and official radiology reports. In the present study, the consistency between EMRs, who have completed 2 years in service, and the final report of the radiologists was examined and a better consistency level was found (90.5%) compared to the relevant studies in the literature.

Although abdominal CT interpretation is an important skill, there are limited number of studies in the literature that have analyzed the ability of EMRs to interpret abdominal CT images and the accuracy of such interpretations. Therefore, our study is one among the limited number of studies.

Study Limitations

The fact that interpretation performed by EMRs of vascular injuries was 0% in our study could be because vascular injuries are rare and are more difficult to interpret on CT images. Recognition of vascular injuries based on CT images requires more expertise and experience, and EMRs would need to improve themselves in this regard. We suggest planning a detailed emergency medicine education in this regard.

Conclusion

A general evaluation of the results obtained in our study suggests that EMRs had an overall good performance in interpreting the patients presented to the ED with trauma, who had undergone abdominal CT for suspected abdominal pathology. The reason for high rate of agreement can be explained by the fact that EMRs are usually the first physicians who meet and treat patients with trauma.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of Bursa Uludağ University Faculty of Medicine (approval number: 2019-6/8, date: 25.03.2019).

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.A.A., Design: S.T.S.C., Data Collection and/or Processing: V.A.D., Analysis and/or Interpretation: D.S., Literature Search: V.A.D., Writing: S.T.S.C., V.A.D., M.Ç.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. White S, Mendicuti DA, Sodickson A, Viscomi S, Stella M, Ledbetter MS. Nontraumatic Emergency Radiology of the Thorax. Emergency Radiology: The Requisites. Ed: Jorge AS. Mosby, Inc an affiliate of Elsevier; 2009.p.234-74.
2. World Health Organization. Global burden of disease. Available from: www.who.int/healthinfo/global_burden_disease/en/ (Cited 2010 May 1)
3. Boullion B, Lefering R, Vorveg M, Tiling T, Neugebauer E, Troidl H. Travma score systems: Colognevalidationstudy. J Travma. 1997;42:652-8.
4. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-center care on mortality. Engl J Med. 2006;354:366-78.
5. Pekdemir M, Cete Y, Eray O, Atilla R, Cevik AA, Topuzoglu A. Epidemiological characteristics of trauma patients. Ulus Travma Derg. 2000;6:250-4.
6. Durdu T, Kavalci C, Yilmaz F, Yilmaz MS, Karakilic ME, Arslan ED, et al. Analysis of trauma cases admitted to the emergency department. J Clin Analytic Med. 2014;5:182-5.
7. Bingol O, Ayrık C, Kose A, Bozkurt S, Narcı H, Ovla D, et al. Retrospective analysis of whole-body multislice computed tomography findings taken in trauma patients. Turk J Emerg Med. 2015;15:116-21.

8. Champion HR, Copes WS, Sacco WJ, Lawnick MM, Keast SL, Bain LW, et al. The Major Trauma Outcome Study: establishing national norms for trauma care. J Trauma. 1990;30:1356-65.
9. Gönültaş F, Kutlutürk K, Gök A, Barut B, Şahin T, Yılmaz S. Analysis of risk factors of mortality in abdominal trauma. Ulus Travma Acil Cerrahi Dergisi. 2020;26:43-9.
10. Makay Ö, Fırat Ö, Gürcü B, Sezer T, İçöz G. Abdominal travmada değişim süreci: Ege Üniversitesi deneyimi. Turk J Surg. 2005:21:4:196-200.
11. Bagheri-Hariri S, Ayoobi-Yazdi N, Afkar M, Farahmand S, Arbab M, Shahlafar N, et al. Abdominal and pelvic CT scan interpretation of emergency medicine physicians compared with radiologists' report and its impact on patients' outcome. Emerg Radiol. 2017;24:675-80.
12. Guven R, Akca AH, Caltili C, Sasmaz MI, Kaykisiz EK, Baran S, et al. Comparing the interpretation of emergency department computed tomography between emergency physicians and attending radiologists: A multicenter study. Nigerian J Clin Pract. 2018;21:1323-9.
13. Mucci B, Brett C, Huntly LS, Greene MK. Cranial computed tomography in trauma: the accuracy of interpretation by staff in the emergency department. Emerg Med J. 2005;22:538-40.
14. Kang MJ, Sim MS, Shin TG, Jo IJ, Song HG, Song KJ, et al. Evaluating the accuracy of emergency medicine resident interpretations of abdominal CTs in patients with non-traumatic abdominal pain. J Korean Med Sci. 2012;27:1255-60.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.06926
Eurasian J Emerg Med. 2022;21(2): 120-5

Diagnostic Accuracy of the Sonographic Ottawa Foot and Ankle Rules for Ankle and Foot Fractures in Emergency Department

Farhad Heydari, Loabat Adib, Saeed Majidinejad, Reza Azizkhani

Department of Emergency Medicine, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Aim: This study was carried out to determine whether the addition of a bedside ultrasound (US) to the Ottawa Foot and Ankle Rules (OAR) could decrease the need for radiographic imaging in the patients presenting to emergency department (ED) with foot and/or ankle trauma.

Materials and Methods: In this prospective observational study, adult patients with acute foot and/or ankle injuries were included. Patients were first examined and OAR results were recorded. Then, US exam was performed by emergency physicians who were blinded to the OAR results. After that, the patients received radiography regardless of OAR exam and US findings. The US and OAR results were then compared to the formal radiography interpretation.

Results: A total of 240 patients with a mean age of 36±12 years were included in the study of which 86 (35.8%) were female. The sensitivity of OAR in detecting foot and/or ankle fractures was 97.5% [95% confidence interval (CI): 86.8 to 99.9%] and the specificity of OAR increased from 48.5 % (95% CI: 41.4 to 55.7%) to 99.5% (95% CI: 97.2 to 100) with the addition of US. The OAR can reduce radiography by 40%, and if ultrasonography was used before radiography, there would be an approximately 72% reduction in X-ray requests.

Conclusion: When used in conjunction with OAR, US can be used by trained physicians in ED to more accurately identify patients who would benefit from having an X-ray performed. US examination can further reduce the ordering of X-rays when compared to using OAR alone.

Keywords: Ultrasonography, foot, ankle, emergency department, injury

Introduction

Foot and ankle injuries in clinical practice are the most common traumatic injuries in patients admitted to the emergency department (ED) (1,2). Findings of ankle and foot injuries are often subtle, and diagnoses may be delayed, especially in cases of multiple trauma (1,3). Although a significant clinical fracture of the ankle or midfoot occurs in less than 15-22%, most patients undergo radiography at ED (4,5).

This small yield led to the introduction of the Ottawa Foot and Ankle Rules (OAR) in 1992 to reduce the radiographs ordered by physicians without adversely affecting the quality of health care (6). These rules were based solely on assessing bone tenderness and weight-bearing. In most cases of isolated ankle trauma, the OAR should be used within 48 hours of injury to determine whether ankle or foot radiographs are necessary (1,2,7).

Assessment of the ankle includes the ability to walk for at least four steps immediately after the injury and at the time of evaluation and notes localized tenderness of the posterior edge of the distal 6 cm or tip of either malleolus. Assessment of the foot includes the ability to walk for at least four steps immediately after the injury and at the time of evaluation and notes localized tenderness of the navicular bone or the base of the fifth metatarsal (1,2,7).

The OAR has a high sensitivity (92-100%) and a modest specificity (10-79%), and its use would lead to significant reduction in the number of radiographs by 30-40% (1,4). Bedside ultrasonography (US) is a reliable and helpful diagnostic tool for fractures in the ED. Ultrasound has many advantages, such as safety, ease of use at the bedside, low cost, availability, mobility, no radiation exposure, and increased patient satisfaction (3,8,9).

Corresponding Author: Loabat Adib, M.D., Department of Emergency Medicine Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
E-mail: loabat.adib@gmail.com ORCID ID: orcid.org/0000-0002-5836-9690

Received: 01.07.2021
Accepted: 15.09.2021

Cite this article as: Heydari F, Adib L, Majidinejad S, Azizkhani R. Diagnostic Accuracy of the Sonographic Ottawa Foot and Ankle Rules for Ankle and Foot Fractures in Emergency Department. Eurasian J Emerg Med. 2022;21(2):120-5.

Emergency medical specialists are among the first-line physicians who are responsible for the management of traumatic patients. When the US is performed by the same person who has previously examined the patient, it provides a quick diagnosis because it can quickly combine images with the patient's history and clinical condition (8-10).

In this regard, studies reported high sensitivity and specificity of US in diagnostics of long bone fractures (11). To date, bedside US has been found to have a sensitivity of 87.3-100% and specificity of 90.1-99.1% in the detection of foot and ankle fractures (12). While OAR has been found to modestly decrease the numbers of unnecessary radiographs taken (1,2,4), few studies have been published regarding the ability of bedside US to further lower the need for X-rays in patients with ankle and midfoot injuries (5).

This study was carried out to determine whether the addition of a bedside US to the assessment process could be performed to decrease the need for radiographic imaging in the patients presenting to the ED with foot and/or ankle trauma.

Materials and Methods

Study Design

This prospective observational study was conducted at the emergency departments of Alzahra and Kashani University Hospital in Isfahan, Iran between November 2017 to May 2019. The study was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.REC.1396.3.988). Oral and written informed consent from all patients were obtained.

Study Setting and Population

All patients older than 16 years and hemodynamically stable who presented to the ED with acute foot and/or ankle injuries were included. Emergency medicine residents evaluated them and recorded the patients' sex, age, the cause of the injury (walking, running, sports, or traffic accident) and clinical data including the OAR results of each patient who met the inclusion criteria.

Patients who were admitted to the ED more than 48 hours after injury, those with an open fracture, or visible major dislocations, or decreased level of consciousness or intoxicated patients, no informed consent, multiple traumas, or diminished sensation related to neurologic deficits, and with a history of prior fracture at the injury site were excluded from the study.

Study Protocol

First, a history was obtained from the patients then they underwent physical examination and OAR findings were recorded. Then, ultrasound examinations by one of the four independent emergency physicians (sonographers) were performed in a standard format based on previously published work (5,9-11) and conducted before radiography. Sonographers were blinded to the OAR results.

Standard radiographies were obtained after the US and OAR examination. The patients in the study received X-ray of the foot and/or ankle regardless of OAR exam and US findings. Radiography results were interpreted by the reporting radiology team who had not visited or examined the patients and were blinded to US results. The OAR, US and X-ray results were then collected using a study checklist. The final assessment of the radiography of the ankle and foot by the reporting radiology team was considered the criterion standard for the diagnosis of a fracture. The ongoing clinical management of the patient was conducted by the primary emergency physicians under hospital protocols. Finally, the US and OAR results were compared to the formal X-ray interpretation. At least 15 days after the initial ED visit, clinical follow-up was performed to determine if an undetected fracture was present.

Each sonographer received a two-hour theoretical and a two-hour of practical training that included basic ankle and foot assessment by another emergency medicine specialist who is experienced in musculoskeletal US. All bedside ultrasonography examinations were conducted by a Philips Affiniti 50 US Machine and a 5-12-MHz linear probe. The US was used for scanning of four regions: proximal of the distal tibia (up to 10 cm), proximal of the distal fibula (up to 10 cm), fifth metatarsal bone (proximal to the distal tip), and navicular bone in the anteromedial aspect of the ankle. The US was performed on the affected areas of the feet and ankles (9-11). The presence of cortical disruption, stepping, or axial deviation on the bone surface were described as a fracture in an ultrasonographic view.

Statistical Analysis

All data were saved and statistical analysis of data was performed using SPSS version 22 software (IBM Corp, Armonk, NY, USA). Qualitative data were expressed as frequencies and percentages, while quantitative data were expressed as the mean and standard deviation (SD). Test characteristics of sensitivity and specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated with 95% confidence interval (CI). A p value less than 0.05 was considered statistically significant.

Results

A total of 240 patients with a mean age of 36±12 years (range: 18-75 years) were included in the study (Figure 1). Of all patients, 86 (35.8%) were female and 154 (64.2%) were male. In 40 patients (16.7%), a total of 42 fractures were detected using radiography

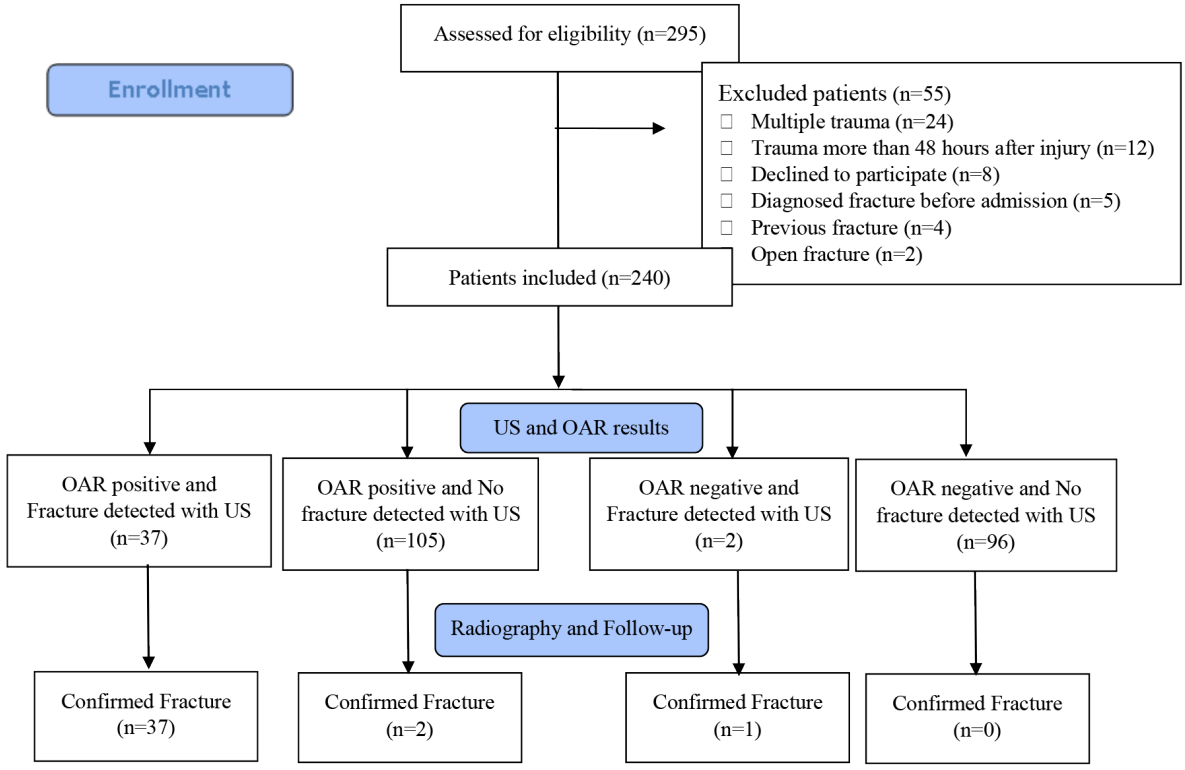

Figure 1. Study flowchart

US: Ultrasound, OAR: Ottawa Foot and Ankle Rules, n: Number

(31% medial malleolus fracture, 28.5% lateral malleolus fracture, 28.5% fifth metatarsal fracture, 4.8% first metatarsal fracture and 4.8% talus and 2.4% posterior malleolus fractures). Two of the patients had bimalleolar fractures (Table 1).

In 40 patients with fractures, 38 (95%) were identified using US, and one talus fracture and one posterior malleolus fracture were missed. Overall, 37 OAR-positive patients (37.7%) were diagnosed with ankle and/or foot fractures by both US and X-ray (Figure 1). In one OAR-negative patient, US revealed an avulsion fracture of the lateral malleolus (Table 2). A significant fracture was defined as having a displacement greater than 3 mm in accordance with the definition used when validating the OAR (5). All missed fractures were insignificant fractures and treated non-surgically.

The sensitivity, specificity, positive predictive value (PPV), and the negative predictive value (NPV) of OAR and US in detecting foot and/or ankle fractures was shown in Table 3. We found that the specificity of OAR increased from 48.5% to 99.5% (95% CI: 97.2 to 100%) with the addition of US.

These results indicate that implementation of OAR can reduce radiography by 40% (97 patients), and if ultrasonography was used before radiography in OAR-positive patients, there would be an approximately 72% reduction in X-ray requests (Table 2).

Discussion

Most patients entering the emergency department with foot and/or ankle trauma are exposed to radiographic examinations. The OAR has a modest specificity (10-79%), and its use would lead to significant reduction in the number of unnecessary radiographs by 30-40% (1). Despite the widespread use of OAR, fractures are seen in less than 15% of patients with ankle and foot trauma (1-4). Therefore, at least 80-85% of X-rays will be negative (3). Foot and ankle injuries are almost universally assessed by the OAR, which has reported a sensitivity of 92% to 100% and a specificity of 10% and 79% for foot and ankle fractures respectively (1,4,13). In this study, the sensitivity and specificity of OAR in detecting significant foot and/or ankle fractures were 97.5 and 48.5 %. Also, a fracture rate of 16.7% was detected. It was similar to the original papers establishing the OAR, which had a positive fracture rate of 17% (1,4,13). One talus fracture and one posterior malleolus fracture were missed. In other studies, fifth metatarsal and distal fibula fracture were missed (4,11,12).

Similar to current study, a systematic review and meta-analysis (n=27) by Bachmann et al. (1) showed that the OAR has a high sensitivity (ranged from 96.4-99.6%) and a modest specificity (ranged from 26.3-47.9%). Its use should reduce radiography

Table 1. Baseline characteristics of the patients				
Variables		**No fracture (n=200)**	**Fracture (n=40)**	**p value**
Age (year)		37.11±12.33	33.87±11.41	0.127
Sex	Male	131 (65.5%)	23 (57.5%)	0.335
	Female	69 (34.5%)	17 (42.5%)	
Location of fracture	Medial malleolus fracture	-	13 (31%)	
	Lateral malleolus fracture	-	12 (28.5%)	
	Fifth metatarsal fracture	-	12 (28.5%)	
	First metatarsal fracture	-	4 (4.8%)	
	Posterior malleolus fractures	-	1 (4.8%)	
	Talus fracture	-	1 (2.4%)	
n: Number				

Table 2. Comparison of US exam and OAR results in fracture detection with X-ray				
Examination results		**X-ray result**		**Total**
		Positive (fracture)	**Negative (no fracture)**	
US exam	Positive	38	1	39
	Negative	2	199	201
OAR	Positive	39	103	142
	Negative	1	97	98
Total		40	200	240
OAR: Ottawa Ankle Rules, US: Ultrasonography				

Table 3. Diagnostic value of ultrasonography and OAR in diagnosis of ankle and/or foot fractures								
Examiner		**Sensitivity (%) (95% CI)**	**Specificity (%) (95% CI)**	**PPV (%) (95% CI)**	**NPV (%) (95% CI)**	**LR+ (95% CI)**	**LR- (95% CI)**	**Accuracy (%) (95% CI)**
OAR		97.5 (86.8-99.9)	48.5 (41.4-55.7)	27.5 (24.7-30.5)	99.0 (93.2-99.9)	1.9 (1.6-2.2)	0.05 (0.01-0.36)	56.7 (50.2-63.0)
US	Overall	95.0 (83.1-99.4)	99.5 (97.2-100)	97.4 (84.3-99.6)	99.0 (96.4-99.7)	190.0 (26.9-1344)	0.05 (0.01-0.19)	98.7 (96.4-99.7)
	Positive OAR	94.9 (82.7-99.4)	100 (96.5-100)	100 (100-100)	99.0 (96.2-99.7)	-	0.05 (0.01-0.20)	99.1 (95.9-100)
PPV: Positive predictive value, NPV: Negative predictive value, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, US: Ultrasonography, OAR: Ottawa Ankle Rules								

by 30-40% in a population with a fracture burden of 15% (1). Finally, Bachmann et al. (1) reported that although there are high sensitivity and good negative LRs with the OAR, differences in physical examination skills, clinical experience, and interpretation of test criteria can affect sensitivity and negative LR.

Another systematic review (n=22) by Jonckheer et al. (2) demonstrated that the sensitivity and specificity of the OAR after an ankle sprain in adults range from 92-100% and from 16-51%, respectively. Several rules and diagnostic processes have been developed to improve the specificity of the OAR and to assist physicians in deciding whether or not to perform radiography (2). Similar to our study, Yazdani et al. (7) showed that in diagnosing ankle and/or foot fractures, the OAR had a sensitivity of 100% and a specificity of 40.50%, and implementation of the OAR had the potential for reducing radiographs by 33%.

Our study demonstrated that the US can be used as a good diagnostic tool for detecting fractures in patients with foot and/or ankle trauma. The US has a sensitivity and specificity of 95.0%, and 99.5%, and the specificity of OAR increased from 48.5% to 99.5% (95% CI: 97.2 to 100) with the addition of US. Also, if US were used before X-ray in OAR-positive patients, there would have been a 72% reduction in X-ray requests.

In a study performed by Canagasabey et al. (5) on 110 patients, they reported that the sensitivity and specificity of US assessment for diagnosing fractures in Ottawa positive patients were 90.9% (95% CI: 65.7 to 98.3), and 90.9% (95% CI: 88.1% to 91.7%), respectively. They showed that if ultrasound is used in patients before radiography, there would be an approximately 80% reduction in radiograph requests (5). In another study by Hedelin et al. (4), 122 patients were examined with US as a triage tool to exclude ankle fractures in the ED by junior orthopedic surgeons. They demonstrated that OAR could exclude the request for radiographs in 23% of patients, whereas US-guided triage could have resulted in a 70% reduction in X-ray requests (4). Similar to our study, one OAR-negative patient had an avulsion fracture of the lateral malleolus on both US and X-ray. The rate of reduction in X-ray requests in these two studies (80% and 70%) is similar to the results of our study (72%).

Ekinci et al. (9) and Atilla et al. (14) stated that the US had good sensitivity and specificity for diagnosing fractures in OAR-positive patients. Tollefson et al. (15) reported that among patients with positive OAR, the specificity of OAR increased from 50% to 100% with the addition of US. In a study by Shojaee et al. (12) the accuracy of US was compared to radiography in patients with a suspected diagnosis of the distal leg or ankle fracture. The sensitivity and specificity of ultrasound were 98.9%, and 86.4% respectively.

Finally, our findings and related studies suggest that if the US assessment for foot and/or ankle fractures in patients were performed prior to radiography, the number of X-rays ordered would be significantly reduced.

Study Limitations

The diagnosis time of the US evaluation was not measured in our study, because the US examination is performed by the same physician who examines the patient. Because this study included US followed by X-ray for all patients, we were not able to compare the rapidity of diagnosis of one modality versus another, nor could we quantify the effect of the imaging modality on the length of stay in the ED. The results of our study cannot be generalized to penetrating injuries, multiple traumas, children, and injuries over one week.

Conclusions

In this study, US had a high sensitivity and specificity for diagnosing ankle and foot fractures. When used in conjunction with OAR, US can be used by trained physicians in the ED to more accurately identify patients who would benefit from having an X-ray performed. US examination can further reduce the ordering of X-rays when compared to using OAR alone.

Acknowledgements

The present article was extracted from the thesis by Dr. Loabat Adib to achieve her specialist degree in emergency medicine from Isfahan University of Medical Sciences. The authors would like to express their gratitude to the staff of the ED of Al-Zahra and Kashani Hospital, Isfahan, Iran.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences (no: IR.MUI.REC.1396.3.988).

Informed Consent: Oral and written informed consent was obtained from all parents, before enrolment into the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.H., L.A., S.M., R.A., Concept: F.H., L.A., S.M., R.A., Design: L.A., F.H., Data Collection or Processing: F.H., L.A., S.M., R.A., Analysis or Interpretation: F.H., L.A., Literature Search: F.H., L.A., S.M., R.A., Writing: L.A., F.H.

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

Financial Disclosure: This study was funded by Isfahan University of Medical Sciences.

References

1. Bachmann LM, Kolb E, Koller MT, Steurer J, ter Riet G. Accuracy of Ottawa ankle rules to exclude fractures of the ankle and mid-foot: systematic review. BMJ. 2003;326:417.
2. Jonckheer P, Willems T, De Ridder R, Paulus D, Holdt Henningsen K, San Miguel L, et al. Evaluating fracture risk in acute ankle sprains: Any news since the Ottawa Ankle Rules? A systematic review. Eur J Gen Pract. 2016;22:31-41.
3. Crosswell S, Leaman A, Phung W. Minimising negative ankle and foot X-rays in the Emergency Department—Are the Ottawa ankle rules good enough? Injury. 2014;45:2002-4.
4. Hedelin H, Goksör L-Å, Karlsson J, Stjernström S. Ultrasound-assisted triage of ankle trauma can decrease the need for radiographic imaging. Am J Emerg Med. 2013;31:1686-9.
5. Canagasabey MD, Callaghan MJ, Carley S. The sonographic Ottawa foot and ankle rules study (the SOFAR study). Emerg Med J. 2011;28:838-40.
6. Stiell IG, Greenberg GH, McKnight RD, Nair RC, McDowell I, Worthington JR. A study to develop clinical decision rules for the use of radiography in acute ankle injuries. Ann Emerg Med. 1992;21:384-90.
7. Yazdani S, Jahandideh H, Ghofrani H. Validation of the Ottawa Ankle Rules in Iran: a prospective survey. BMC Emerg Med. 2006;6:1-7.
8. Zamani M, Mazaheri M, Heydari F, Masoumi B. Comparison of diagnostic accuracy of bedside ultrasonography and radiography for calcaneal fractures in the emergency department. Journal of Emergency Practice and Trauma. 2021;7:17-21.
9. Ekinci S, Polat O, Günalp M, Demirkan A, Koca A. The accuracy of ultrasound evaluation in foot and ankle trauma. Am J Emerg Med. 2013;31:1551-5.
10. Champagne N, Eadie L, Regan L, Wilson P. The effectiveness of ultrasound in the detection of fractures in adults with suspected upper or lower limb

injury: a systematic review and subgroup meta-analysis. BMC Emerg Med. 2019;19:1-15.

11. Crombach A, Azizi N, Lameijer H, El Moumni M, Ter Maaten JC. Point-of-care bedside ultrasound examination for the exclusion of clinically significant ankle and fifth metatarsal bone fractures; a single blinded prospective diagnostic cohort study. J Foot Ankle Res. 2020;13:1-7.
12. Shojaee M, Hakimzadeh F, Mohammadi P, Sabzghabaei A, Manouchehrifar M, Dolatabadi AA. Screening characteristics of ultrasonography in detection of ankle fractures. Emergency. 2016;4:188.
13. Wu J, Wang Y, Wang Z. The diagnostic accuracy of ultrasound in the detection of foot and ankle fractures: a systematic review and meta-analysis. Medical Ultrasonography. 2021;23:203-12.
14. Atilla OD, Yesilaras M, Kilic TY, Tur FC, Reisoglu A, Sever M, et al. The accuracy of bedside ultrasonography as a diagnostic tool for fractures in the ankle and foot. Acad Emerg Med. 2014;21:1058-61.
15. Tollefson B, Nichols J, Fromang S, Summers RL. Validation of the Sonographic Ottawa Foot and Ankle Rules (SOFAR) Study in a Large Urban Trauma Center. J Miss State Med Assoc. 2016;57:35-8.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.02350
Eurasian J Emerg Med. 2022;21(2): 126-31

Implementing a Simulation-Based Distance Learning Model: How to Facilitate High-Engagement Experiential Training While Reducing the Risk of Infectious Disease Transmission Amongst Healthcare Professionals

Héctor Alonso[1], Maria Soledad Holanda[2], Liébana Piedra[3], Ignacio Del Moral[4], Jose M. Maestre[4]

[1]Department of Emergency Medicine, Marques de Valdecilla University Hospital, and Simulation Instructor, Valdecilla Virtual Hospital, Santander, Spain
[2]Department of Intensive Care Unit, Marques de Valdecilla University Hospital, and Simulation Instructor, Valdecilla Virtual Hospital, Santander, Spain
[3]Department of Emergency Medicine, Sierrallana Hospital, and Simulation Instructor, Valdecilla Virtual Hospital, Santander, Spain
[4]Valdecilla Virtual Hospital, Santander, Spain

Abstract

Aim: We aim to describe and evaluate a new model for distance experiential learningin order to help reduce the transmission risk among professionals envolved in education activities.

Materials and Methods: In April 2020, in partnership with our hospital's Emergency Department Educational Leadership, Valdecilla Virtual Hospital tested and introduced an experiential distance learning model. Professionals wanted to engage from their homes without having to travel to a simulation facility.

Results: Between July 1 and 22, 2020 we ran seven courses following this new model of course. Each one consisted of a two-hour session on two consecutive days. There were 44 participants whose ages ranged from 26 to 53 years (average=40), 62% identified as female, and 68% reported working at the emergency department, 19% at the cardiology unit, 7% in primary care, and 5% in internal medicine. We evaluated the content validity, feasibility and acceptability of the model. The results of an anonymous survey filled in at the end of the course showed they considered the distance training model as realistic (92%), easy to use (95%), well-organized (94%), an engaging educational tool (94%), and desirable for practising in the future (94%).

Conclusion: These results may encourage the educational community to develop more programs using this new approach of "taking care of patients from a distance" not only during a pandemic, but also on a regular basis. We think this model can achieve positive results using distance clinical simulation combining their traditional simulation technology to address the training needs of their healthcare organization.

Keywords: Simulation, emergency, COVID-19

Introduction

Healthcare simulation is a widely used method for training healthcare professionals that contributes to the long-term retention of acquired complex, technical, clinical and teamwork skills. Translational science research shows that measured outcomes transfer to improved patient care practices and improved patient and public health. Simulated training can also yield a favorable return on financial investment (1).

Healthcare simulation subscribes to the theory of experiential learning that a two-dimensional cycle is necessary for learning to occur. The first dimension involves perception, whereby the learner begins by grasping a specific experience or concept. The second dimension involves processing the concept: in this phase, the learner transforms the experience through reflection and active experimentation (2). To complete this cycle, learners and educators usually meet on site to participate in highly interactive,

Corresponding Author: Hector Alonso Valle, PhD, Department of Emergency Medicine, Marques de Valdecilla University Hospital, and Simulation Instructor, Valdecilla Virtual Hospital, Santander, Spain
E-mail: hectoravt@telefonica.net ORCID ID: orcid.org/0000-0002-6070-8874
Cite this article as: Alonso H, Holanda MS, Piedra L, Del Moral I, Maestre JM. Implementing a Simulation-Based Distance Learning Model: How to Facilitate High-Engagement Experiential Training While Reducing the Risk of Infectious Disease Transmission Amongst Healthcare Professionals. Eurasian J Emerg Med. 2022;21(2):126-31.

Received: 10.06.2021
Accepted: 19.09.2021

high-fidelity clinical scenarios using mannequins, actors, task trainers, or a combination of these figures. These sessions are followed by debriefing (3). The rapid development of technology-assisted learning methods has gained momentum since the Coronavirus disease-2019 (COVID-19) pandemic, helping reduce the risk of transmission among professionals and opening up new alternatives for remote experiential learning (4).

The best approach to implementing clinical simulation activities in this context has not yet been determined. Several solutions have been proposed to bring the pieces together in a way that would allow professionals to continue their training activities, while simultaneously protecting the clinical safety of the participants, avoiding, as far as possible, the spread of coronavirus. These include a variety of simulation-based asynchronous (e.g. recorded videos, vignettes, serious games) and synchronous (e.g. webinars, team collaboration) methods, recreating the clinical environment with different levels of fidelity and learner engagement, and offering a series of reflection strategies (5). Innovations in healthcare simulation technologies can now also provide the learner with opportunities to practice increasingly complex motor, decision-making and communication skills using virtual patient simulation. Dynamic health conditions can be created in a variety of clinical settings that respond to user interventions and help improve learning satisfaction when compared to a case-based learning approach. Using virtual patient simulation to provide simulation-based distance learning experiences that are extremely realistic and highly interactive for the learner remains a challenge. Communicating with patients, family members and healthcare workers, performing physical examinations on patients, monitoring physiological parameters, and evaluating complementary examinations in an actual clinical environment are all limited by mathematical algorithms and software capabilities. A mix of synchronous on-site/on-line distance learning methods may recreate the richness and complexity of a true clinical experience and facilitate reflection on action promoting participant engagement, while limiting exposure to infectious diseases during a pandemic. Our aim is to describe and evaluate a model for distance experiential learning, where participants see simulated patients remotely and interact with other caregivers, and subsequently analyze the session in a debriefing (6).

Materials and Methods

In April 2020, Valdecilla Virtual Hospital, in partnership with our hospital's emergency department and intensive care educational leadership, tested and introduced an experiential distance learning model in response to requests from physicians all over Spain for simulation-based clinical training in the midst of the pandemic. Professionals wanted to engage from their homes without having to travel to a simulation facility, thus effectively preventing possible contagion derived from the COVID-19 pandemic.

The team: Valdecilla Virtual Hospital, Santander, Spain is a nonprofit, charitable organization that offers instructor and clinical training courses with tuition. It is an educational institute accredited by the American College of Surgeons and affiliated to the Center for Medical Simulation, Boston, USA. Its aim is to achieve superior clinical education programs, enhance patient safety, and promote simulation (7).

The instructional design model followed the Analysis, Design, Development, Implementation and Evaluation (ADDIE) model (8).

Analysis: Unstable heart disease is one of the most common reasons for presentation to the emergency department and was identified as a point of special interest among the target students (9). This type of visit allows participants to effectively interact, but does not require a large number of interventional maneuvers that would be unfeasible to conduct from their homes.

Design: Delivery methods and types of learning activities were selected. Zoom was chosen as a widely available, straightforward platform that allows users to switch back and forth between different types of teaching methods (e.g., live video feed, lectures, small group discussions). Participants connected remotely to a live simulated emergency room, and attended simulated patients while interacting with other caregivers who were present in the scenario. Simulated interactions were followed by an instructor-led debriefing to reflect on clinical performance (Figure 1).

Development: This included creating the instructional content, a prototype, and assessment instruments. Learning objectives were both clinical (establishing the initial approach and providing training on the key premises and complications of the unstable cardiac patient) and behavioral (leadership and effective communication in emergency situations). The prototype included the following phases:

Pre-briefing: this was intended to establish a psychologically safe container that allowed trainees to engage actively in simulation and to display meaningful learning behaviors during post-simulation debriefing conversations (e.g., openly discuss errors or divergent ideas without fear of negative implications) (10). During this phase, the instructor introduced the simulation learning experience and set the tone for the rest of the session, specifically: 1) clarifying objectives, environment, roles, confidentiality, and expectations; 2) establishing a fiction contract (i.e., reaching a collaborative and explicit agreement among

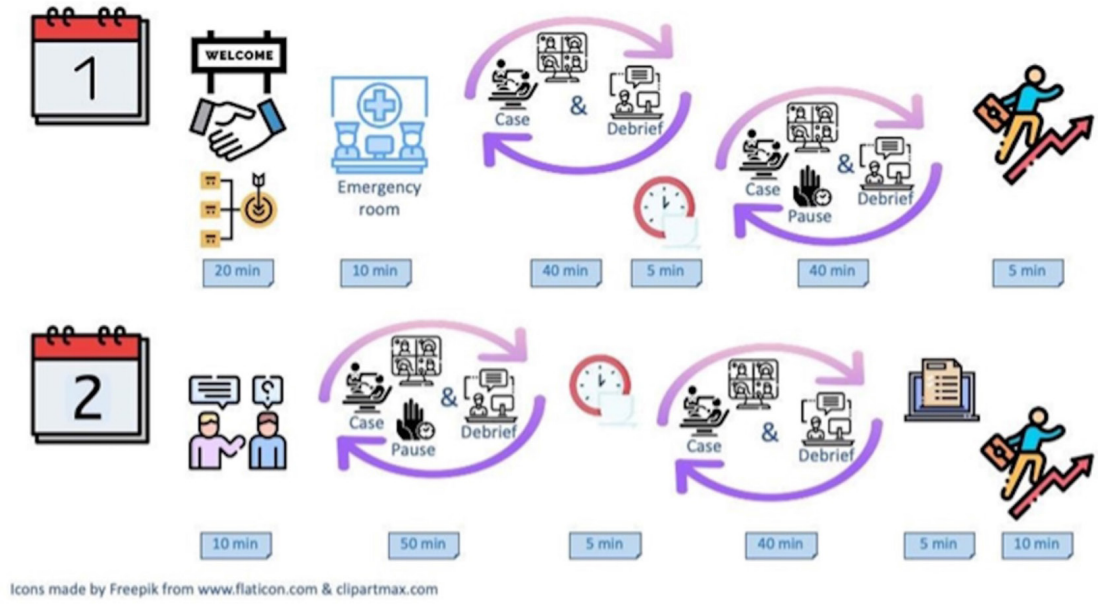

Figure 1. Course timeline

instructors and trainees to commit to playing fair with respect to fidelity and realism); 3) housekeeping (e.g., platform instructions for the videoconference, agenda, breaks); and 4) expressing commitment to respecting learners and understanding their perspective (11).

Introduction to the clinical environment and distance interaction: In this phase, participants connected live to the emergency room to meet the nurse and resident who were assisting them in carrying out tasks during the scenario, and to observe how the instructor interviewed a patient. They also became familiar with monitors, requesting additional tests, and calling for assistance. Interactive Zoom platform features were also explained to the participants.

Case briefing and clinical scenario: Two participants saw the patient in each case, and the others participated as observers. One of the instructors briefly introduced the case and then two participants interacted remotely with the patient and healthcare providers who were on site at the simulated emergency room.

Debriefing: Instructors and learners reflected on the simulation experience with the purpose of moving toward assimilation and adaption of learning in future situations (Figure 2). In the debriefing, we used the good judgment method that takes into account the expert opinion of the instructors, while simultaneously valuing the unique perspective of the trainees in order to learn what drives their behaviors, so that both their mistakes and successes can be understood (12).

Summary: At the end of each session, we collaborated with participants to summarize take-away messages that may improve their practice.

Results

Between July 1 and 22, 2020, we ran seven courses. Each one consisted of a two-hour session on two consecutive days. There were 44 participants whose ages ranged from 26 to 53 years (average=40), 62% identified as female, and 68% reported working in the emergency department, 19% in the cardiology unit, 7% in primary care, and 5% in internal medicine. Two simulation technology specialists participated. One assisted with the online platform and the other controlled the mannequin and live audiovisual settings during simulations. The nurse and resident not only prepared the cases but also acted as healthcare providers in order to help participants attend the patient and meet the objectives of the simulation. One instructor assisted with the clinical aspects of the cases and co-debriefed, while the other kept participants oriented and led the debriefing session. High-fidelity simulators from

different vendors were used for the cases, while the room set-up resembled a tertiary hospital emergency room (Figure 1). Each course simulated four different cases. Two had a "linear structure" in which the patient developed clinical complications and participants diagnosed and treated them in real time with no interruptions. The other two cases were paused twice to facilitate in-action reflection and to discuss patient care and the diagnostic and therapeutic measures to be taken, regardless of participants' performance. Pauses lasted three to five minutes and the simulated providers took care of the patient who remained stable. When participants fulfilled the objectives, the instructor terminated the case.

Metrics: We evaluated the content validity, feasibility and acceptability of the model, as follows:

Content validity is the extent to which the content of a simulation is representative of the knowledge or skills that have to be learnt for application in the real environment. The course was coordinated by two clinical educators. We applied a modified Delphi technique using four sequential interviews combined with three pilot programs to define the aspects of the simulated environment, including the emergency room environment, patient characteristics, monitoring, equipment, simulated providers, teleconferencing, telephone communications and complementary tests available (12). Three physicians (two emergency room and one intensive care), four cardiologists, two nurses, one nurse assistant, three simulation specialists and two educators participated, all of whom had between five and twenty years of experience in designing simulation-based courses. Everyone had to be in agreement for a component to be incorporated into the simulation model.

Feasibility evaluates all relevant project factors to determine whether the plan of action is likely to produce the anticipated result. We analyzed the benefit of the operational, technical, financial, and educational capabilities of the project in terms of economics and organization.

Acceptability explores participants' experience with the model, the perceived realism, and their opinion on whether it efficiently achieves the desired teaching goals. The results of an anonymous survey (Figure 3) completed at the end of the course showed that they judged the distance training model to be realistic (92%), easy to use (95%), well-organized (94%), an engaging educational tool (94%), and desirable for practicing in the future (94%). The survey contained some open-ended questions in which the learners could comment on relevant aspects of the course. Table 1 shows some representative comments shared by participants at the end of the session.

Discussion

Due to the COVID-19 pandemic, remote learning simulation has become a new element for simulation in university hospitals. The performance of this new model and possible difficulties are reviewed below.

Evaluation: We included formative assessment to facilitate learning, using the good judgment method during debriefing to reflect on participants' performance. This helped reveal the internal frames of trainees (including knowledge, assumptions, and emotions) that drove their actions during the cases (13-16). The instructor helped participants to maintain or reframe those drivers, and to take action to maintain results or achieve better outcomes in the future (1).

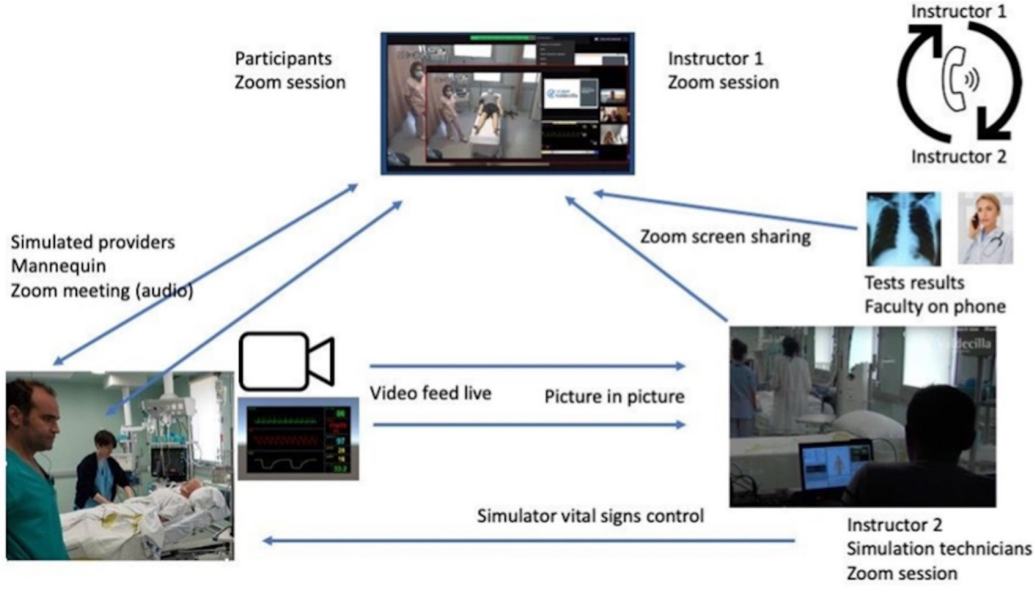

Figure 2. Technical assembly

Table 1. Participants' comments	
Methodology	*"Cases were surprisingly interactive!* *"The novelty is doing everything virtually! And I love the take-home final messages!* *"Quite a fun and novel mini cardio review!"* *"I managed to understand the complexity of making critical decisions"*
Dynamics groups of job	*"I find the "mini-room" tool very useful to pause and think"* *"Being from the same hospital, it's an opportunity to practice together"* *"I realize how important it is to have an explicit leader!"* *"What I liked the most about the course were the small pauses to discuss with the rest of the colleagues who are watching the case from outside, and therefore they have more time to think"*
Duration	*"I would not mind if it was longer, maybe sessions lasting a few weeks."* *"Time flew by!"* *"It was a bit short, considering that online interaction takes some more."*
Technical aspects	*"Transfer of complementary tests (especially with ultrasound) take time to upload"* *"Do any writing and images on the virtual white board"* *"We had no problem with the connection!"* *"Patient voice sometimes was difficult to understand"*

Satisfaction Questions	Nº	1	2	3	4	5	Total
I have received information about the general objectives of the course	1	0	0	1	10	26	37
The course has achieved the proposed objectives	2	0	0	0	5	30	35
The course content has corresponded to what was expected when enrolling	3	0	0	0	3	34	37
The level of knowledge with which the topics have been treated has been adequate	4	0	0	0	5	30	35
I consider that the course has given me new knowledge	5	0	0	0	7	30	37
The teaching methodology of this course has been adequate	6	0	0	0	3	33	36
The documentation provided has been useful and updated	7	0	1	5	7	24	37
The course has been well organized	8	0	0	0	2	34	36
The conditions of the classrooms and the equipment have been adequate	9	0	0	0	5	32	37
The course is of interest to my professional activity	10	0	0	0	1	36	37
I would recommend attending this course to my colleagues	11	0	0	0	2	34	36
I am satisfied with having completed this course	12	0	0	0	0	36	36

Figure 3. Satisfaction rating

Hurdles

Technology: A hidden danger was viewing simulation solely as technology, since it does not facilitate learning alone. Simulation is an educational methodology and once the learning needs are identified, the instructional design must be properly planned and the technology must then be appropriately aligned to achieve the objectives [Technological Pedagogical Content Knowledge (TPACK) Framework] (17,18). Most of the challenges were related to the participants' equipment, especially connection issues and background noise during the sessions.

Maintaining an engaging learning environment: The main challenges were creating experiences that are realistic for the participants and facilitating involvement during cases and debriefing. Key elements to address these issues were setting and discussing expectations, modeling the interaction with the simulated providers during the scenario, being able to talk to the patient and observing changes in vital signs online, encouraging people to speak up, and fostering respectful disagreement. It was also important to discuss the origin of the cases, and to interact in a high-fidelity environment that resembles a "real scenario" with medications, defibrillators, monitoring, and other commonly used elements.

Where to start: The basic principle is to generate a training tool that maintains the essence of simulated clinical practice but which allows participants not to be personally present in the simulation room in order to guarantee their safety in the

midst of the COVID-19 pandemic. This model can achieve positive results using remote clinical simulation combined with traditional simulation technology to address the training needs of healthcare organizations.

Conclusion

Distant learning combining on-site simulation technology with teleconferencing software based on experiential learning principles is feasible and easy to implement. This modality is well-accepted by participants for acute care training in the emergency room. These results may encourage the educational community to develop more programs using this new approach of "remote patient care" not only during pandemics, but also in our daily work. It seems likely that this new model will be able to facilitate future learning courses in the health field.

Ethics

Ethics Committee Approval: Since the article does not include patients there was not ethics committee decision.

Informed Consent: All the participants were informed about the new training method previously and accepted to be included.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.A., M.S.H., I.D.M., J.M.M., Design: H.A., M.S.H., I.D.M., Data Collection and/or Processing: H.A., M.S.H., L.P., I.D.M., Analysis and/or Interpretation: H.A., M.S.H., L.P., I.D.M., J.M.M., Literature Search: H.A., M.S.H., L.P., I.D.M., J.M.M., Writing: H.A., M.S.H., L.P., I.D.M., J.M.M.

Conflict of Interest: The authors declare that they have no financial relationship with any commercial company of products or services related to simulation. Valdecilla Virtual Hospital is affiliated with the Center for Medical Simulation, Boston, USA. Both are nonprofit, charitable, educational institutions offering tuition-based clinical and educator training programs.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. McGaghie WC, Draycott TJ, Dunn WF, Lopez CM, Stefanidis D. Evaluating the impact of simulation on translational patient outcomes. Simul Healthc. 2011;6 Suppl(Suppl):S42-7.
2. Armstrong E, Parsa-Parsi R. How can physicians' learning styles drive educational planning? Acad Med. 2005;80:680-4.
3. Del Moral I, Maestre JM. A view at the practical application of simulation in 15 professional education. Trends Anaesth Crit Care. 2013;3:146-51.
4. Kerfoot BP, Baker H. An online spaced-education game for global continuing medical education: a randomized trial. Ann Surg. 2012;256:33-8.
5. Verkuyl M, Lapum JL, Hughes M, McCulloch T, Liu L, Mastrilli P, et al. Virtual gaming simulation: exploring self-debriefing, virtual debriefing, and in-person debriefing. Clin Simul Nursing. 2018;20:7-14.
6. Rojo E, Torres B, de la Fuente A, Oruña C, Villoria F, Del Moral I, Maestre JM. La simulación como herramienta para facilitar el cambio en las organizaciones sanitarias [Simulation as a tool to facilitate change in healthcare organisations]. J Healthc Qual Res. 2020;35:183-90.
7. Padilha JM, Machado PP, Ribeiro A, Ramos J, Costa P. Clinical Virtual Simulation in Nursing Education: Randomized Controlled Trial. J Med Internet Res. 2019;21:e11529.
8. Khalil MK, Elkhider IA. Applying learning theories and instructional design models for effective instruction. Adv Physiol Educ. 2016;40:147-56.
9. Kontos MC, Diercks DB, Kirk JD. Emergency department and office-based evaluation of patients with chest pain. Mayo Clin Proc. 2010;85:284-99.
10. Roussin CJ, Larraz E, Jamieson K, Maestre JM. Psychological safety, self-efficacy, and speaking up in interprofessional health care simulation. Clin Simul Nursing. 2018;17:38-46.
11. Rudolph JW, Raemer DB, Simon R. Establishing a safe container for learning in simulation: the role of the presimulation briefing. Simul Healthc. 2014;9:339-49.
12. Rudolph JW, Simon R, Dufresne RL, Raemer DB. There's no such thing as "nonjudgmental" debriefing: a theory and method for debriefing with good judgment. Simul Healthc. 2006;1:49-55.
13. Normand SL, McNeil BJ, Peterson LE, Palmer RH. Eliciting expert opinion using the Delphi technique: identifying performance indicators for cardiovascular disease. Int J Qual Health Care. 1998;10:247-60.
14. Brett-Fleegler M, Rudolph J, Eppich W, Monuteaux M, Fleegler E, Cheng A, Simon R. Debriefing assessment for simulation in healthcare: development and psychometric properties. Simul Healthc. 2012;7:288-94.
15. Rudolph JW, Simon R, Raemer DB, Eppich WJ. Debriefing as formative assessment: closing performance gaps in medical education. Acad Emerg Med. 2008;15:1010-6.
16. Maestre JM, Rudolph JW. Theories and styles of debriefing: the good judgment method as a tool for formative assessment in healthcare. Rev Esp Cardiol (Engl Ed). 2015;68:282-5.
17. Koehler MJ, Mishra P. What is technological pedagogical content knowledge (TPACK)? Contemporary Issues in Technology and Teacher Education 2009;9:60-70.
18. Martin-Parra JI, Manuel-Palazuelos JC, Maestre JM, Gómez-Fleitas M, del Moral I. Changing the paradigm in health care education: Hospital virtual Valdecilla. J Surg Educ. 2014;71:142-6.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.45467
Eurasian J Emerg Med. 2022;21(2): 132-7

Can Spesific Biomarkers Be Used to Enlighten the Major Mechanisms of Acute High Dose Diclofenac Sodium-Related Nephrotoxicity?

Sinem Doğruyol[1], İlker Akbaş[2], Abdullah Osman Koçak[3], Serpil Aygörmez[4], Habip Emrah Leylek[5], Sultan Tuna Akgöl Gür[3], Özge Ertener[6]

[1]Department of Emergency Medicine, Manisa Merkez Efendi State Hospital, Manisa, Turkey
[2]Department of Emergency Medicine, Bingöl State Hospital, Bingöl, Turkey
[3]Department of Emergency Medicine, Atatürk University Faculty of Medicine, Erzurum, Turkey
[4]Department of Biochemistry, University of Kafkas Faculty of Veterinary Medicine, Kars, Turkey
[5]Department of Emergency Medicine, Bandırma State Hospital, Balıkesir, Turkey
[6]Department of Pathology, İzmir University of Economics Faculty of Medicine, İzmir, Turkey

Abstract

Aim: The aim of this study was to examine the basic mechanisms that play a role in the acute nephrotoxicity caused by diclofenac sodium.

Materials and Methods: Only water was given to the control group; however, the diclofenac sodium group was group intoxicated by giving water-soluble, 240 mg/kg, oral single dose diclofenac sodium. After 24 hours, all animals were sacrificed and histopathological analyzes were performed. The levels of spesific biomarkers [vascular endothelial growth factor (VEGF), nuclear factor-kappa B (NF-κB), matrix metalloproteinase-9 (MMP-9), metalloproteinase tissue inhibitor-1 (TIMP-1) and carcinoembryonic antigen (CEA)] that may be related to the nephrotoxicity mechanism were evaluated.

Results: As a result of biochemical analysis, we found that VEGF, TIMP-1, NF-κB and CEA levels were significantly higher and MMP-9 levels were significantly lower in diclofenac sodium group compared to control group. Nephrotoxicity related histopathological changes were observed in the sections of diclofenac sodium group.

Conclusion: This study has shown that the biomarkers we evaluated in the diclofenac sodium-induced acute high-dose intoxication model we created can help us to identify the nephrotoxicity and to explain the nephrotoxicity mechanism with the three main steps (the hemodynamic-related pathway, the inflammation-related pathway, and the oxidative stress-related pathway). With a simple version of this panel adapted to emergency departments, we may be able to diagnose diclofenac sodium-related nephrotoxicity.

Keywords: Diclofenac sodium, intoxication, nephrotoxicity

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently preferred drugs with their analgesic and antipyretic properties. They are also widely used in acute and chronic inflammation (1). Diclofenac sodium as a NSAID inhibits cyclooxygenase (COX) also known as prostaglandin endoperoxide synthase, reversible. Thus, it shows analgesic and anti-inflammatory activity by reducing the production of prostaglandin and thromboxane A2 (2). In addition to being a non-selective (both COX-1 and COX-2 enzymes) inhibitor of COX, diclofenac sodium causes a decrease in the level of leukocyte intracellular free arachidonic acid. This situation is associated with the decrease in fatty acid levels released from the cell (3).

Similar to all NSAIDs on the market, diclofenac sodium is commonly available over the counter, which may be the main reason for the increase in overdose-related organ damage cases (4). People with acute overdose due to diclofenac sodium may have serious clinical manifestations such as convulsions, metabolic acidosis, coma, acute renal failure and acute liver failure (5). Although

Corresponding Author: Sinem Doğruyol, M.D., Department of Emergency Medicine, Manisa Merkez Efendi State Hospital, Manisa, Turkey
E-mail: dogruyolsinem@gmail.com ORCID ID: orcid.org/0000-0002-6949-7233
Cite this article as: Doğruyol S, Akbaş İ, Koçak AO, Aygörmez S, Leylek HE, Akgöl Gür ST, Ertener Ö. Can Spesific Biomarkers Be Used to Enlighten the Major Mechanisms of Acute High Dose Diclofenac Sodium-Related Nephrotoxicity? Eurasian J Emerg Med. 2022;21(2):132-7.

Received: 25.06.2021
Accepted: 28.09.2021

some progress has been made in understanding diclofenac sodium-related mechanisms of organ toxicity, the pathways in the process of renal toxicity have not been fully elucidated (6). It is possible to classify the mechanisms that are thought to be associated with acute damage mainly under the following 3 headings; hemodynamics associated pathway (renal perfusion disorder), immune-mediated inflammation of the interstitium (Acute interstitial nephritis or Glomerulopathy) and oxidative stress (OS) (6-8).

Vascular endothelial growth factor (VEGF) is a powerful endothelial cell mythogen that supports angiogenesis, increases vascular permeability and is chemotactic for monocytes. VEGF embryogenesis plays an important role in placenta growth, tumor growth, diabetes, wound healing, inflammatory response and tissue regeneration. VEGF, a glycoprotein of 45 kDa, is synthesized in podocytes and tubular epithelium. Antiprostaglandin activity and vasoconstriction due to non-selective COX enzyme inhibition cause hypoxia that increases VEGF. Although it is known that hypoxia is the main stimulation that increases VEGF synthesis; factors such as prostaglandins, mechanical stress, hyperglycemia and reactive oxygen species (ROS) are thought to cause an effect in the same direction (9). Conversely, VEGF levels were found to decrease in antineoplastic-related nephrotoxicity with endothelial and glomerular damage (10).

Nuclear factor-kappa B (NF-κB) is a nuclear transcription factor that acts as an inflammatory regulator. NF-κB induces the release of inflammatory mediators that play an important role in the OS-related damage mechanism, especially TNF-α (11). With this activation of NF-κB, it is thought that it plays a role in the formation of nephrotoxicity by leading the cell to apoptosis and death (12). Likewise, in the diclofenac-induced intoxication model, it was observed that NF-κB activation and NF-κB-dependent proinflammatory cytokine production were induced in mice. This process led to apoptosis of kidney cells (13,14).

Matrix metalloproteinases (MMP) is a family of enzymes synthesized in the kidney from glomerular cells, mesenchymal cells and tubular epithelium (15). The MMP enzyme family consists of four different groups: collagenases (MMP-1, -8, -13, -18), stromelins (MMP-3, -7, -10, -11, -12), gelatinases (MMP-2, -9) and membrane type MMPs (MT-MMP-14, -15, -16, -17) (16). Among these, MMP-9 has been shown to increase in experimentally created nephrotoxicity and renal fibrosis (17). The main reason for this increase is that MMP-9 is induced by increased TNF-α in case of OS. Metalloproteinase tissue inhibitor-1 (TIMP-1) has been defined as the main inhibitor of MMP-9. MMP-9 and TIMP-1 are cytokines that play an important role in the formation of inflammation in the parenchymal organs. It is also known that the balance between these two biomarkers is disturbed in the disease settings accompanied by renal scarring, which is associated with drugs and diabetes, especially immunosuppressives (18). Carcinoembryonic antigen (CEA) is a glycoprotein that plays a role in cell adhesion. CEA is normally produced in gastrointestinal tissue during fetal development, but production stops before birth. Today, it is used as a tumor marker for the diagnosis and treatment of adenocarcinoma and colorectal cancers (19). It is usually found at very low levels in the blood of healthy adults. In contrast, CEA 'serum levels' was found to be abnormally high in cases such as hepatic cirrhosis/inflammation, cardiometabolic diseases, pulmonary emphysema, rectal polyps, colon inflammation and chronic kidney diseases (20-22). The increase in CEA in these non-neoplastic diseases is thought to be associated with inflammation (23).

In our study, we aimed to create a setting of oral, high dose diclofenac sodium intoxication for suicidal purposes that we often encounter in the emergency departments. In the literature, nephrotoxicity patients due to chronic and therapeutic diclofenac sodium intake were examined but the mechanism of nephrotoxicity was not clearly explained (24,25). Our main goal in our study was to evaluate the roles of specific biomarkers in the diagnosis of diclofenac sodium-induced nephrotoxicity and to define the main steps of the nephrotoxicity mechanism using these biomarkers. For this purpose, we evaluated the levels of biomarkers (VEGF, NF-κB, MMP-9, TIMP-1, and CEA) within 24 hours that may be related to the nephrotoxicity mechanism.

Materials and Methods

The study was started with the permission obtained from Kafkas University Local Ethics Committee for Animal Experiments (KAU-HADYEK/2020-025). A total of 14, 4-6-month-old female Wistar Albino breed rats were used in the study. All animals were fed as ad libitum. The rats were housed in an environment with an automatically adjusted light with a 12/12 hours cycle of light/dark. Before starting work, the rats were kept for seven days for the adaptation process. After the adaptation process, the rats were divided into two groups, with 7 rats in each group. We referred to the study of Dass (26) for toxication model. Diclofenac sodium tablet (Dicloron®, Deva 50 mg tablet) was used in this study.

Groups;

Control group: Only water was given orally.

Diclofenac sodium group: The group intoxicated by giving water-soluble, 240 mg/kg, oral single dose diclofenac sodium.

24 hours after the application of diclofenac sodium, kidney

tissue samples required for analysis were collected after animals were sacrificed through the use of cervical dislocation under anesthesia [ketamine hydrochloride (75 mg/kg) (Ketalar®, Pfizer, New York, United States), and xylazine (15 mg/kg) (Rompun®, Bayer, Leverkusen, Germany) intramuscular] in accordance with ethical rules. After the kidney tissues were homogenized, they were centrifuged at 3000 rpm and their homogenate was separated. The separated homogenates were placed in Ependorf tubes and stored at -20 °C until the time of analysis.

Biochemical Analysis

Tissue samples were homogenized with phosphate buffer (pH=7.4) and then, centrifuged at 3000 rmp for five minutes. The homogenates obtained were stored at -20 °C until the time of analysis. Total protein analysis and gram protein calculation was performed according to the method developed by Lowry et al. (27) from the homogenates of kidney tissue. VEGF, NF-κB, MMP-9, TIMP-1, and CEA analyses were done according to the kit procedure using the commercial ELISA kit (ELISA- YL Biotech Company, Shanghai, China). The data taken after the ELISA measurement were calculated with the previously determined protein analysis data and the data were given in grams of protein. Serum creatinine values were measured at the end of 24 hours to evaluate renal functions. To explain the nephrotoxicity mechanisms associated with diclofenac sodium, biomarkers were associated with three basic steps: hemodynamics-related pathway, inflammation-related pathway, and OS-related pathway.

Histopathological Analysis

Renal tissue samples collected from the experimental rats were fixed in neutral buffered 10% formalin. Following routine tissue follow-up procedures, sections with a thickness of 4 µm were taken from the prepared paraffin blocks. Hematoxylin and eosin (H&E) stain was applied to the sections to identify the histopathological changes.

Statistical Analysis

Unpaired t-test analysis was conducted for all the biochemical parameters to test whether there is a difference between the two groups. An experiment-wise p value of ≤0.05 was deemed to be statistically significant throughout the study. All the analyses were conducted using GraphPad 8.1 (GraphPad Software Inc., San Diego, CA, USA).

Results

Biochemical Results

VEGF, NF-κB, MMP-9, TIMP-1, and CEA parameters determined as a result of the analyses were given in Figure 1A-E, respectively. VEGF levels, which played an important role in renal perfusion, were higher in the diclofenac sodium group compared to the control group. We found that this difference between the two groups was statistically significant (p=0.001). When MMP-9 and its inhibitor TIMP-1, which play a role in the OS-related damage mechanism, were examined; we found that the mean MMP-9 levels were lower in the diclofenac sodium group compared to the control group. This difference between two groups was statistically significant (p=0.003). TIMP-1 levels were statistically significantly higher in the diclofenac sodium group than in the control group (p=0.007). We found that average levels of NF-κB, another OS-related biomarker, were also higher in the diclofenac sodium group. This difference was statistically significant (p=0.006). We found that CEA levels, which are biomarkers

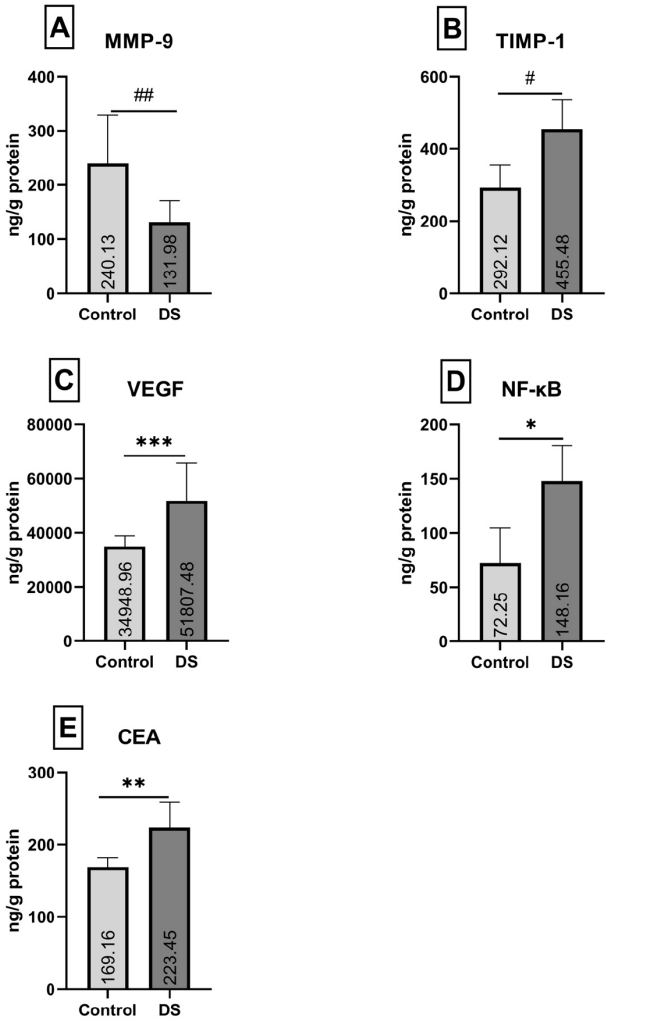

Figure 1. Means and Standarts Errors of the two groups for biochemical parameters (A, B, C, D, E). *p=0.006, **p=0.002, ***p=0.001, #p=0.007, ##p=0.003

MMP-9: Matrix metalloproteinase-9, TIMP-1: Metalloproteinase tissue inhibitor-1, VEGF: Vascular endothelial growth factor, NF-κB: Nuclear factor-kappa B, CEA: Carcinoembryonic antigen, DS: Diclofenac sodium group

associated with inflammation, were statistically significantly higher in the diclofenac sodium group than in the control group (p=0.002). We also found that the creatinine values measured at the end of the experiment in the diclofenac sodium group were significantly higher than the control group [the mean difference: 0.48, 95% confidence interval (CI): 0.39-0.57; p<0.001].

Histopathological Results

In histopathological examinations, no pathological finding was observed in the sections belonging to the control group, except mild congestion and erythrocyte extravasation, which were thought to be related with resection. Additional to mild congestion, interstitial edema and mixed type inflammatory infiltrate containing interstitial neutrophils and lymphocytes were observed in kidney histopathology of rats induced with diclofenac sodium. Focal tubular damage and degenerative changes were also detected in these histopathological sections of diclofenac sodium group (Figure 2).

Discussion

The primary outcome of this study was to explain the basic mechanisms that play a role in the nephrotoxicity model due to acute high dose diclofenac sodium intake that we have created in rats. For this purpose, we evaluated three main mechanisms which are the most associated with non-steroidal anti-inflammatory drugs (NSAID) nephrotoxicity; the hemodynamic-related pathway (renal perfusion impairment), the inflammation-related pathway, and the OS-related pathway. In order to evaluate the role of these classified mechanisms in diclofenac sodium nephrotoxicity, we investigated the biomarkers associated with these pathways. We examined the level changes of these biomarkers in a short period of 24 hours, which provide easy use in emergency services because they are produced as a kit.

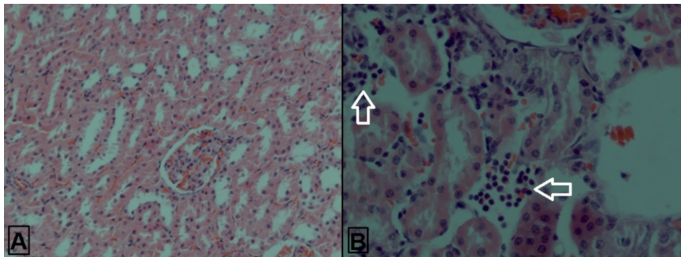

Figure 2. Kidney histopathology: A) Control group shows normal kidney morphology with minimal congestion and erythrocyte extravasation (H&E staining, x200). B) Diclofenac sodium induced nephrotoxicity group shows interstitial edema and mixed type inflammatory infiltrate containing interstitial neutrophils and lymphocytes (H&E staining, x400). Focal tubular damage and degenerative changes were also detected in these histopathological sections (white arrows)

H&E: Hematoxylin and eosin stain

Diclofenac sodium, as a NSAID, is a highly used drug that is sold as analgesic and as antipyretic, both as prescription drugs and over the counter purchases (3). This is also the main reason why we often encounter diclofenac sodium-related toxicity cases in emergency departments. Although the potential to cause multiorgan toxicity of diclofenac sodium is known, its mechanisms remain unknown (8). In studies in the literature, it was agreed that the main cause of the diclofenac sodium-related acute kidney injury setting may be perfusion disorder developed as a result of vasoconstriction (4,28). This condition was associated with antiprostaglandin activity caused by non-selective COX enzyme inhibition, which is the most fundamental feature of diclofenac sodium (29). In this mechanism, defined as "hemodynamics-related pathway", hypoxia is the main stimulant, and the role of VEGF released in response to hypoxia has often been studied in the literature (30,31). Various growth factors and cytokines, such as epidermal growth factor, are active in the expression of VEGF in transformative growth factor β (TGF-β), platelet-induced growth factor (PDGF), insulin-like growth factor I (IGF-I), angiotensin II, interleukin-1 (IL-1) and IL-6. VEGF can also be induced by prostaglandins, mechanical stress, hyperglycemia, protein kinase C (PKC) and ROS (32). In renal tissue with diclofenac sodium-induced nephrotoxicity, the main cause of the increase in VEGF has been associated with hypoxia (33). There are studies in the literature showing that there may be an increase in VEGF levels in drug-related nephrotoxicity models (34-37). However, there is no NSAID-related acute high dose toxicity data in the literature. Similar to our study, Kaur and Sanyal (38) applied diclofenac sodium at a dose of 8 mg/kg per oral (18 weeks). At this dose of diclofenac sodium intake, VEGF levels were found to be low, similar to the control group. In our study, we found that VEGF levels were significantly higher in acute diclofenac sodium toxicity group. We believe that this increase in VEGF levels in our study may be a guide for understanding the main "hemodynamic and circulatory-related" toxicity mechanism in diclofenac sodium-related nephrotoxicity.

Cytochrome P450 mediated metabolization of diclofenac sodium is an inducer for ROS production (25). Increased ROS triggers the formation of OS reactions, thus damaging cellular macromolecules and leading to cell death (39). Oxidative stress is one of the main pathways in the mechanism of kidney damage. There are studies indicating that there is up-regulation in the activity of NF-κB in many cells due to damage caused by the OS-related ROS response (40,41). In our study, we found that NF-κB increased significantly in the group developing nephrotoxicity due to acute diclofenac sodium. In the literature, we did not encounter a study examining NF-κB levels in acute high-dose diclofenac sodium-induced nephrotoxicity model similar to our study. However, a study of different nephrotoxicity models linked

to cadmium and chemotherapeutics has shown that levels of NF-κB increase in toxicity groups (42).

Other biomarkers we examined in our study due to their activities in the OS-related nephrotoxicity mechanism were MMP-9 and its inhibitor TIMP-1. It has been stated in the literature that TNF-α, one of the cytokines known as the OS marker and found to have increased in the diclofenac-induced renal toxicity, induced the release of MMP-9 (24). It can be observed that MMP-9 levels vary in different ways as the clinical situation of acute kidney injury changes. In their study, Caron et al. (43) found that MMP-9 levels increased in AKI due to ischemia perfusion damage, while TIMP-1 levels decreased. However, this picture can be reversed in chronic kidney diseases associated with glomerulosclerosis or tubulointerstitial fibrosis. Sharma et al. (44) found that MMP-9 levels decreased and TIMP-1 levels increased in the unilateral ureteral obstruction model they created in their study. Unlike the literature, we found that MMP-9 levels were low and TIMP-1 levels were significantly higher in the nephrotoxicity-related AKI model we created in our study.

Inflammation is known to be one of the main mechanisms involved in the development of acute kidney injury process. While nephrotoxic drugs generally cause inflammation in the glomerulus, proximal tubules and surrounding cellular matrix, it is known that in NSAID-induced nephrotoxicity acute interstitial nephritis also play a role in this process (45). However, this process, which is associated with drug-related inflammation in the literature, has often been associated with chronic NSAID usage (46). CEA, which we examined in our study, is widely used as a tumor marker. However, there have been recent studies that CEA levels are also high in low-grade chronic inflammation-related conditions such as atherosclerosis, type 2 diabetes and metabolic syndrome (47,48). It is thought that this low-grade chronic inflammation process, which is also seen in chronic kidney diseases, may explain why CEA shows high blood levels (49). In our study, we believe that high CEA levels are associated with 'inflammation-related pathways' in diclofenac sodium-related nephrotoxicity. However, the increase in CEA levels we found occurred in a short period of 24 hours, and it occurred in a much shorter time compared to the chronic inflammation process mentioned in the literature.

Conclusion

This study has shown that the biomarkers we evaluated in the diclofenac sodium-induced acute high-dose intoxication model we created can help us to identify the nephrotoxicity and to explain the nephrotoxicity mechanism with the three main steps. Of these biomarkers, a statistically significant decrease has been observed in the MMP-9 levels in the diclofenac sodium group compared to the control group whereas there has been a significant increase in the VEGF, TIMP-1, NF-κB and CEA levels in the diclofenac sodium group compared to the control group. With a simple version of this panel adapted to emergency departments, we may be able to diagnose diclofenac sodium-related nephrotoxicity and refer patients to appropriate centers. In addition, in the light of the parameters we examine, we think that understanding the basic mechanisms that play a role in the diclofenac sodium-related kidney injury can be a guide in the research for specific treatments.

Ethics

Ethics Committee Approval: The study was started with the permission obtained from Kafkas University Local Ethics Committee for Animal Experiments (KAU-HADYEK/2020-025).

Informed Consent: Animal experiment.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and/or Medical Practices: S.A., Ö.E., Concept: İ.A., A.O.K., S.T.A.G., Design: İ.A., S.T.A.G., Data Collection and/or Processing: A.O.K., H.E.L., Ö.E., Analysis and/or Interpretation: S.D., Literature Search: S.D., H.A.L., Writing: S.D., İ.A.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Aydin G, Gökçimen A, Öncü M, Çicek E, Karahan N, Gökalp O. Histopathologic changes in liver and renal tissues induced by different doses of diclofenac sodium in rats. Turkish J Vet Anim Sci. 2003;27:1131-40.
2. FitzGerald GA, Patrono C. The coxibs, selective inhibitors of cyclooxygenase-2. N Engl J Med. 2001;345:433-2.
3. Baravalia Y, Vaghasiya Y, Chanda S. Hepatoprotective effect of Woodfordia fruticosa Kurz flowers on diclofenac sodium induced liver toxicity in rats. Asian Pac J Trop Med. 2011;4:342-6.
4. Sales GTM, Foresto RD. Drug-induced nephrotoxicity. Rev Assoc Med Bras. 2000;66(Suppl. 1):s82-s90.
5. Mousa AA, Elweza AE, Elbaz HT, Tahoun EAE, Shoghy KM, Elsayed I, et al. Eucalyptus Globulus protects against diclofenac sodium induced hepatorenal and testicular toxicity in male rats. J Tradit Complement Med. 2019;10:521-8.
6. El-Shafei RA, Saleh RM. Pharmacological effects of vitamin C & E on diclofenac sodium intoxicated rats. Biomed Pharmacother. 2016;84:314-22.
7. Choudhury D, Ahmed Z. Drug-induced nephrotoxicity. Med Clin North Am. 1997;81:705-17.
8. Hickey EJ, Raje RR, Reid VE, Gross SM, Ray SD. Diclofenac induced in vivo nephrotoxicity may involve oxidative stress-mediated massive genomic DNA fragmentation and apoptotic cell death. Free Radic Biol Med. 2001;31:139-52.

9. Schrijvers BF, Flyvbjerg A, De Vriese AS. The role of vascular endothelial growth factor (VEGF) in renal pathophysiology. Kidney Int. 2004;65:2003-17.
10. Estrada CC, Maldonado A, Mallipattu SK. Therapeutic inhibition of VEGF signaling and associated nephrotoxicities. J Am Soc Nephrol. 2019;30:187-200.
11. Vyas D, Laput G, Vyas AK. Chemotherapy-enhanced inflammation may lead to the failure of therapy and metastasis, OncoTargets Ther. 2014;7:1015.
12. Khames A, Khalaf MM, Gad AM, Abd El-Raouf OM, Kandeil MA. Nicorandil combats doxorubicin-induced nephrotoxicity via amendment of TLR4/P38 MAPK/NFκ-B signaling pathway. Chem Biol Interact. 2019;311:108777.
13. Fattori V, Borghi SM, Guazelli CFS, Giroldo AC, Crespigio J, Bussmann AJC, et al. Vinpocetine reduces diclofenac-induced acute kidney injury through inhibition of oxidative stress, apoptosis, cytokine production, and NF-κB activation in mice. Pharmacol Res. 2017;120:10-22.
14. Borghi SM, Fattori V, Ruiz-Miyazawa KW, Bertozzi MM, Lourenco-Gonzalez Y, Tatakihara R.I, et al. Pyrrolidine dithiocarbamate inhibits mouse acute kidney injury induced by diclofenac by targeting oxidative damage, cytokines and NF-κB activity. Life Sciences. 2018; 208:221-31.
15. Sant B, Rao PL, Nagar DP, Pant SC, Bhasker ASB. Evaluation of abrin induced nephrotoxicity by using novel renal injury markers. Toxicon. 2017;131:20-8.
16. Öztürk ÖG. Matrix Metalloproteinase Enzyme Family. Arch Med Rev J. 2013;22:209-20.
17. Marti HP. Rôle des métalloprotéases matricielles dans la progression des lésions rénales (Role of matrix metalloproteinases in the progression of renal lesions). Presse Med. 2000;29:811-7.
18. Chromek M, Tullus K, Hertting O, Jaremko G, Khalil A, Li Y-H, et al. Matrix metalloproteinase-9 and tissue inhibitor of metalloproteinases-1 in acute pyelonephritis and renal scarring. Pediatr Res. 2003;53:698-705.
19. Hammarström S. The carcinoembryonic antigen (CEA) family: structures, suggested functions and expression in normal and malignant tissues. In: Seminars in cancer biology. Academic Press, 1999;67-81.
20. Rani BS, Suchitra MM, Rao PS, Kumar VS. (2019). Serum tumor markers in advanced stages of chronic kidney diseases. Saudi J Kidney Dis Transpl. 2019;30:898.
21. Mittal A, Farooqui SM, Pyrtuh S, Poudel B, Sathian B, Yadav SK. Efficacy of carcinogenic embryonic antigen in differential diagnosis of diseases of pancreas and liver–a comparative study in a tertiary care hospital of Western Nepal. Asian Pac J Cancer Prev. 2012;13:275-7.
22. Tong HL, Dong ZN, Wen XY, Gao J, Wang B, Tian YP. Impact of chronic kidney disease on serum tumor markers concentrations. Chin Med J. 2013;126:274-9.
23. Kwon YJ, Lee HS, Shim JY, Lee YJ. Serum carcinoembryonic antigen is positively associated with leukocyte count in Korean adults. J Clin Lab Anal. 2018;32:e22291.
24. Jerine Peter S, Evan Prince S. Diclofenac-induced renal toxicity in female Wistar albino rats is protected by the pre-treatment of aqueous leaves extract of Madhuca longifolia through suppression of inflammation, oxidative stress and cytokine formation. Biomed Pharmacother. 2018;98:45-51.
25. Ahmed AY, Gad AM, El-Raouf OMA. Curcumin ameliorates diclofenac sodium-induced nephrotoxicity in male albino rats. J Biochem Mol Toxicol. 2017;31:e21951.
26. Dass E. Diclofenac-induced liver toxicity in albino rats: dose-dependent study. Indian J Res. 2018;7:49-51.
27. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem. 1951;193:265-75.
28. Naughton CA. Drug-induced nephrotoxicity. Am Fam Physician. 2008;78:743-50.
29. Laurence LB, Bruce AC, Björn CK, Goodman&Gilman's, The Pharmacological Basis of Therapeutics, 11th Ed. TheMcGraw-Hill; 2006.
30. Lucas GNC, Leitão ACC, Alencar RL, Xavier RMF, Daher EDF, Silva Junior GBD. Pathophysiological aspects of nephropathy caused by non-steroidal anti-inflammatory drugs. Braz J Nephrol. 2019;41:124-30.
31. Yuan HT, Li XZ, Pitera JE, Long DA, Woolf AS. Peritubular capillary loss after mouse acute nephrotoxicity correlates with down-regulation of vascular endothelial growth factor-A and hypoxia-inducible factor-1 alpha. Am J Pathol. 2003;163:2289-301.
32. Schrijvers BF, Flyvbjerg A, De Vriese AS. The role of vascular endothelial growth factor (VEGF) in renal pathophysiology. Kid Int. 2004;65:2003-17.
33. Makav M, Gelen V, Gedikli S, Atilla Uslu G, Uslu H, Eroğlu HA. Therapeutic effect of Tarantula cubensis extract on indomethacin induced gastric ulcers in rats. Thai J Vet Med. 2020;50:559-66.
34. Hoffmann D, Fuchs TC, Henzler T, Matheis KA, Herget T, Dekant W, et al. Evaluation of a urinary kidney biomarker panel in rat models of acute and subchronic nephrotoxicity. Toxicology. 2010;277:49-58.
35. Shihab FS, Bennett WM, Yi H, Andoh TF. Expression of vascular endothelial growth factor and its receptors Flt-1 and KDR/Flk-1 in chronic cyclosporine nephrotoxicity. Transplantation. 2001;72:164-8.
36. Peng W, Chen J, Jiang Y, Shou Z, Chen Y, Wang H. Non-invasive detection of acute renal allograft rejection by measurement of vascular endothelial growth factor in urine. J Int Med Res. 2007;35:442-9.
37. Wakelin SJ, Marson L, Howie SE, Garden J, Lamb JR, Forsythe JL. The role of vascular endothelial growth factor in the kidney in health and disease. Nephron Physiology. 2004;98:p73-9.
38. Kaur J, Sanyal SN. Diclofenac, a selective COX-2 inhibitor, inhibits DMH-induced colon tumorigenesis through suppression of MCP-1, MIP-1α and VEGF. Mol Carcinog. 2011;50:707-18.
39. Dolanbay T, Makav M, Gul HF, Karakurt E. The effect of diclofenac sodium intoxication on the cardiovascular system in rats. Am J Emerg Med. 2021;46: 560-6.
40. Li N, Karin M. Is NF-kappaB the sensor of oxidative stress? FASEB J 1999;13:1137-43.
41. Jiao D, Jiang Q, Liu Y, Ji L. Nephroprotective effect of wogonin against cadmium-induced nephrotoxicity via inhibition of oxidative stress–induced MAPK and NF-κB pathway in Sprague Dawley rats. Hum Exp Toxicol. 2019;38:1082-91.
42. Hamad R, Jayakumar C, Ranganathan P, Mohamed R, El-Hamamy MM, Dessouki AA, et al. Honey feeding protects kidney against cisplatin nephrotoxicity through suppression of inflammation. Clin Exp Pharmacol Physiol. 2015;42:843-8.
43. Caron A, Desrosiers RR, Langlois S, Beliveau R. Ischemia-reperfusion injury stimulates gelatinase expression and activity in kidney glomeruli. Can J Physiol Pharmacol. 2005;83:287-300.
44. Sharma AK, Mauer SM, Kim Y, Michael AF. Altered expression of matrix metalloproteinase-2, TIMP, and TIMP-2 in obstructive nephropathy. J Lab Clin Med. 1995;125:754-61.
45. Kim SY, Moon A. Drug-induced nephrotoxicity and its biomarkers. Biomol Ther. 2012;20:268.
46. Perazella MA. Drug-induced renal failure: update on new medications and unique mechanisms of nephrotoxicity. Am J Med Sci. 2003;325:349-62.
47. Ishizaka N, Ishizaka Y, Toda E, Koike K, Yamakado M, Nagai R. Are serum carcinoembryonic antigen levels associated with carotid atherosclerosis in Japanese men? Arterioscler Thromb Vasc Biol. 2008;28:160-5.
48. No JI, Yang JY, Hyun HJ, Yeon CS, Choi HJ. Factors associated with serum levels of carcinoembryonic antigen in healthy non-smokers. Korean J Fam Med. 2013;34:413-9.
49. Huang CS, Huang LK, Chen CY, Wang WS, Yang SH. Prognostic value of postoperative serum carcinoembryonic antigen levels in colorectal cancer patients with chronic kidney disease. Am J Surg. 2021;221:162-7.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.44711
Eurasian J Emerg Med. 2022;21(2): 138-45

Evaluation of Patients Admitted to the Emergency Department with the Suspect of Acute Renal Colic with the Modified STONE Score

Birdal Güllüpınar[1], Pınar Ayvat[2], Erden Erol Ünlüer[1], Serhat Koran[3]

[1]Clinic of Emergency, İzmir Bozyaka Training and Research Hospital, University of Health Sciences Turkey, İzmir, Turkey
[2]Department of Anesthesiology and Reanimation, İzmir Democracy University Faculty of Medicine, İzmir, Turkey
[3]Department of Family Medicine, Istanbul Medipol University Faculty of Medicine, İstanbul, Turkey

Abstract

Aim: Renal colic pain is one of the most common agonizing forms of pain that is frequently treated in emergency departments. Computed tomography (CT), which is used for the detection of kidney stones, is a costly application. Therefore, scoring systems that predict stone have been developed. This study was conducted to investigate the diagnostic accuracy of the Modified STONE Score (MSS) to predict stones.

Materials and Methods: Among those who applied to the emergency department with renal colic pain, patients with CT were examined. Three hundred and thirty-seven patients included in the study were divided into two groups as those with and without kidney stones. It was examined whether there was a difference between these two groups in terms of personal, seasonal, laboratory findings and MSS.

Results: We found that ureteral stone history, pain duration less than 6 hours, presence of hematuria and nausea/vomiting, C-reactive protein (CRP) value below 0.5 mg/dL, The MSS above 9, age ≤50 years were factors that increase stone. The MSS was significantly high in the stone-detected group. When the STONE score is calculated for all patients and divided into three groups (low, moderated, and high modified STONE scores), the prevalence of ureteral stones increases towards the high MSS group.

Conclusion: We found that the modified STONE score was quite successful in predicting ureteral stones. We determined that emergency physicians can diagnose stones using this score and avoid unnecessary CT. The diagnostic value of this score may increase when nausea/vomiting factor is added.

Keywords: Modified STONE Score, urinary tract stones, emergency departments

Introduction

Renal colic pain is a painful urologic case caused by the presence of stones in the urinary tract. Typically, the pain is blunt, continuous, and excruciating, with abrupt onset at the costo-vertebral angle, radiating to the groin and genitals (1). Renal colic pain affects more than 1 million patients who visit hospitals due to complaints from it each year (2) Almost half of these patients revisit hospitals within five to seven years after the first visit. More than 70% of kidney stone occurrences are observed in people aged 20 to 50 years, and the incidence in men is about two times higher than in women (3-5). In Turkey, the prevalence of ureteral stones was reported at approximately 14% (6).

Urinalysis, laboratory tests and imaging methods such as ultrasonography (USG) or computed tomography (CT) are used in renal colic. Although USG can accurately detect hydronephrosis and perinephric fluid, it has low sensitivity in showing and locating kidney stones (7). Non-contrast CT is the gold standard imaging method in the initial diagnosis of patients with ureteral stones (8). In recent years, CT with a sensitivity of 96.6% and a specificity of 94.9% has been the first-choice method as it can detect any hydroureter, hydronephrosis or ureteral edema associated with the location and size of the stone (8,9). Unlike USG, CT exposes patients to high levels of radiation and increases the long-term risk of cancer (10-13). It is estimated that there are new cancer patients due to unnecessary abdominal and pelvic CT scans (14). Therefore, various scoring systems such as STONE score, Modified

Corresponding Author: Asst. Prof. Pınar Ayvat, Department of Anesthesiology and Reanimation, İzmir Democracy University Faculty of Medicine, İzmir, Turkey
E-mail: drpinarunde@yahoo.com ORCID ID: orcid.org/0000-0002-9941-3109

Received: 29.06.2021
Accepted: 10.11.2021

Cite this article as: Güllüpınar B, Ayvat P, Ünlüer EE, Koran S. Evaluation of Patients Admitted to the Emergency Department with the Suspect of Acute Renal Colic with the Modified Stone Score. Eurasian J Emerg Med. 2022;21(2):138-45.

STONE Score (MSS) and CHOKAI Score have been developed to prevent unnecessary CT use and thus reduce radiation exposure in patients with ureteral stones (15-17). The STONE score has a sensitivity of 71.7% and a specificity of 64.7%, while the sensitivity and specificity of the MSS are reported as 87.7% and 70.6% (17). For this reason, many researchers preferred to use MSS.

Although there are many studies on the STONE Score in the literature, there are few studies evaluating the MSS. This study was conducted to investigate the diagnostic accuracy of the MSS and its ability to predict the presence of ureteral stones.

Materials and Methods

This study was designed as a single-center, retrospective observational study and it was carried out in İzmir Bozyaka Training and Research Hospital which has a capacity of 700 beds and an annual average of 200,000 patients. Inclusion criteria for patients were: Applied to emergency department between January 2019 and January 2020, aged 18 and older, had CT scans and diagnosed with renal colic in the emergency department. The person choosing the patient was blind to the study and just did this job. Exclusion criteria for patients were: Being younger than 18 years old, not having a CT scan, having a history of trauma, presence of active malignancy, presence of known renal disease (creatinine >1.5 mg/dL), patients with unavailable or missing laboratory data, presence of leukocytes in urine microscopy and having fever more than 37.7 °C. Demographic data (age, gender, season of application) were retrieved using the hospital information management system database. The diagnosis of patients who came to the hospital with renal colic complaints, was made by anamnesis, physical examination, laboratory findings, abdominal USG and/or abdominal tomography. The patients included in the study were divided into two groups as those with and without ureteral stones. MSS was used in patients with ureteral stones. The MSS is calculated according to the values: Gender (male-3 points), duration of pain (<6 hours-3 points), presence of hematuria (6 points), previous stone history (2 points), C-reactive protein (CRP): <5 mg/L-2 points. Afterwards, the patients were divided into three groups as low risk between 0-4 points, medium risk between 5-9 points, and high risk between 10-16 points. In addition, as in the study of Kim et al. (16), we determined the optimum cut-off value for MSS as 10. According to this cut-off value, we divided them into two groups as MSS positive and MSS-negative. The accuracy rate in the prediction of ureteral stones was examined in all groups.

Statistical Analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) program was used in the analysis of variables. Whether the data were suitable for normal distribution was evaluated with the Shapiro-Wilk test. Independent-samples t-test was used together with Bootstrap results to compare two independent groups with each other according to quantitative data. Mann-Whitney U test was used in conjunction with Monte Carlo results. Pearson chi-square test was tested with Monte Carlo Simulation technique to compare categorical variables with each other. Column ratios were compared with each other and expressed according to Benjamini-Hochberg corrected p value results. Odds ratio with 95% confidence intervals was used to compare patients with and without a risk factor. In order to determine the causal relationship of the presence of ureteral stone with explanatory variables, logistic regression test was tested with the Enter method. Sensitivity and specificity ratios were analyzed by receiver operating curve (ROC) curve analysis to determine the relationship between the real classification and the classification calculated with the cut off values according to the MSS, age and CRP variables. Quantitative variables were shown in the tables as mean (standard deviation) and median (percentile 25/percentile 75), and categorical variables as n (%). Variables were analyzed at 95% confidence level, and p value less than 0.05 was considered statistically significant.

Results

Of 1165 patients admitted to the emergency department with suspected acute renal colic, 337 met the inclusion criteria (Figure 1).

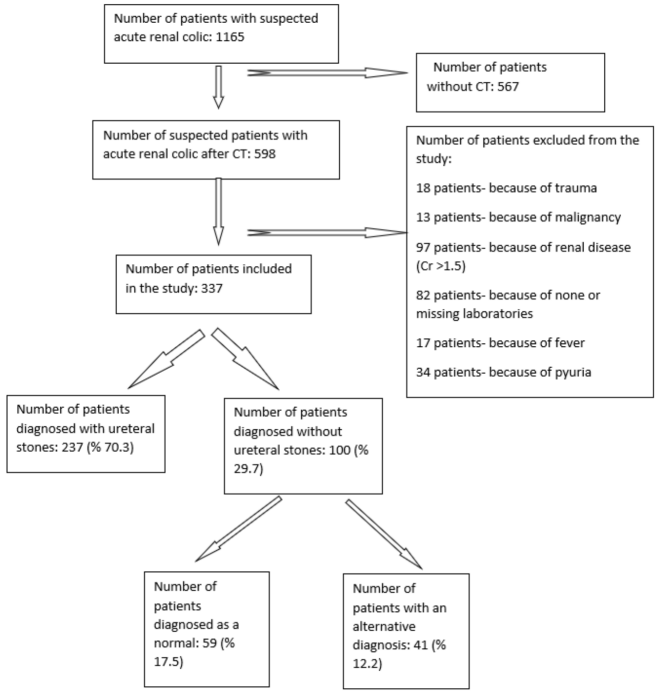

Figure 1. Flow diagram of the study

CR: Creatinine, CT: Computed tomography

In this study, the median (percentile 25/percentile 75) age was 41 (33/52) and the number of male patients was 226 (67.1%). Pain duration was less than six hours in 59.3% of the patients, and it was accompanied by nausea and/or vomiting in 55.5%. Those with a history of ureteral stone in the past were 41.2%. The most common laboratory finding was hematuria with 70.0%. According to CT scan findings, ureteral stones were detected in 237 (70.3%) patients. History of ureteral stone, pain duration less than 6 hours, presence of hematuria, CRP value below 0.5 mg/dL, and STONE score above 9 were significantly more common in the group with ureteral stones (p<0.001). In addition, a statistically significant difference was found in the stone-detected group compared to the stone-free group in terms of age (≤50) and the presence of nausea and/or vomiting (p=0.011, p=0.008). While the median (minimum/maximum) value of the MSS was 12 (11/14) in the stone-detected group, it was 4.5 (3/6) in the other group, and the difference between the groups was statistically significant (p<0.001). No significant difference was found between the groups in terms of leukocyte count (<12.000 cells/mL), BUN (<26 mg/dL) value and creatinine (<1.2 mg/dL) value, the time for application to hospital and gender (p>0.05) (Table 1), (Figure 2). Logistic regression test revealed that 3 factors were statistically significant (p<0.001): Age ≤50 [odds ratio (OR)=5.542], presence of nausea and vomiting (OR=6.83), MSS >9 (OR=100.048) were associated with the incidence of renal stone (Table 2).

According to the MSS, 233 (69.1%) patients were in the high-risk group, 56 (16.6%) patients in the moderated risk group, and 48 (14.2%) patients in the low-risk group. The prevalence of ureteral stones was 227/233 (97.4%) in the high-risk group, 10/56 (17.8%) in the moderated-risk group, and 0/48 (0%) in the low-risk group. As we move from the low-risk group to the high-risk group, the prevalence of ureteral stones increases (Figure 3).

When the MSS cut-off value was accepted as 10, those with MSS 9 and below were called MSS-negative, those with MSS 10 and above were called MSS-positive. The relationship between the diagnosis of renal stones and the diagnosis of alternative diseases between these two groups is shown in Figure 4.

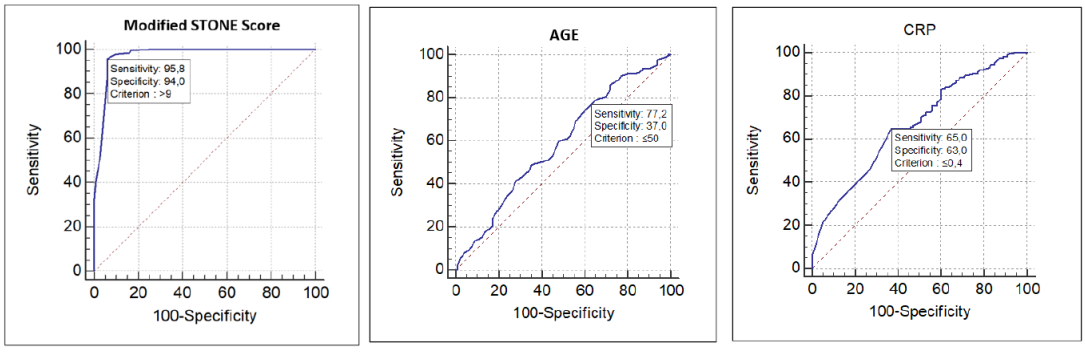

Figure 2. ROC curves about Modified STONE Score, age and CRP level of the patients

ROC: Receiver operating characteristics, CRP: C-reactive protein

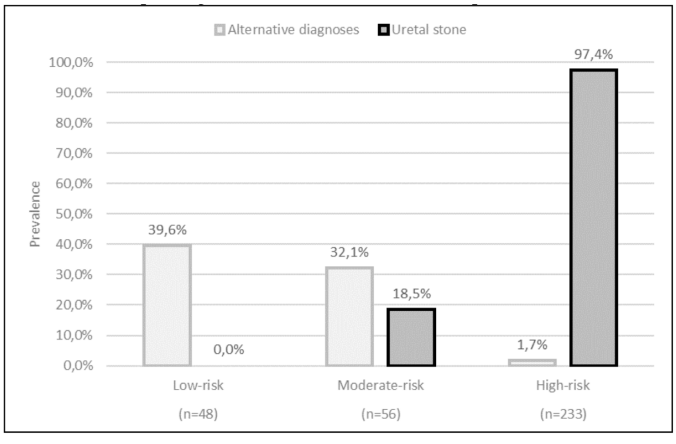

Figure 3. Comparison of patients with low, moderated and high modified STONE Scores in terms of detection of ureteral stones and alternative diagnoses

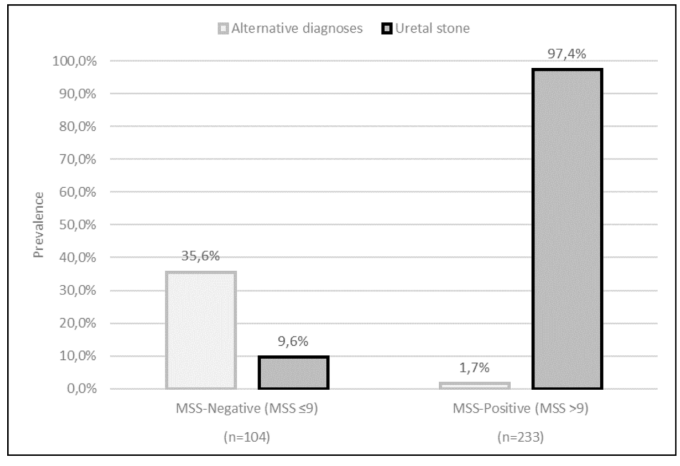

Figure 4. Comparison of patients with positive and negative modified STONE Scores in terms of detecting ureteral stones and alternative diagnoses

MSS: Modified STONE Score

Table 1. Comparison of demographic data, laboratory findings, Modified STONE Score findings of patients with and without ureteral stone

	Total	Patients without stone	Patients with stone	p value
	(n=337)	(n=100)	(n=237)	
Age, median (q1/q3)	41 (33/52)	43 (35/56)	40 (32/50)	**0.011[u]**
Gender, n (%)				
Female	111 (32.9)	40 (40.0)	71 (30.0)	0.077[c]
Male	226 (67.1)	60 (60.0)	166 (70.0)	
Season, n (%)				
Autumn	73 (21.7)	21 (21.0)	52 (21.9)	0.354[c]
Winter	87 (25.8)	30 (30.0)	57 (24.1)	
Spring	69 (20.5)	15 (15.0)	54 (22.8)	
Summer	108 (32.0)	34 (34.0)	74 (31.2)	
Pain duration, n (%)				**<0.001[c]**
<6	200 (59.3)	25 (25.0)	175 (73.8)[A]	8.5 (4.9-14.5)[OR]
>6	137 (40.7)	75 (75.0)[B]	62 (26.2)	
Nausea, vomiting, n (%)				**0.008[c]**
No	150 (44.5)	56 (56.0)[B]	94 (39.7)	1.9 (1.2-3.1)[OR]
Yes	187 (55.5)	44 (44.0)	143 (60.3)[A]	
Stone story, n (%)				**<0.001[c]**
No	198 (58.8)	82 (82.0)[B]	116 (48.9)	4.7 (2.7-8.4)[OR]
Yes	139 (41.2)	18 (18.0)	121 (51.1)[A]	
Hematuria, n (%)				**<0.001[c]**
No	101 (30.0)	83 (83.0)[B]	18 (7.6)	59.4 (29.2-120.7)[OR]
Yes	236 (70.0)	17 (17.0)	219 (92.4)[A]	
Creatinine, mean (SD)	1.1 (0.2)	1 (0.2)	1.1 (0.2)	0.485[t]
BUN, median (q1/q3)	31 (25/37)	30.5 (24/40)	31 (25/37)	0.893[u]
Urea, median (q1/q3)	66.34 (53.5/79.18)	65.27 (51.36/85.6)	66.34 (53.5/79.18)	0.893[u]
CRP, median (q1/q3)	0.4 (0.2/3.7)	1.6 (0.3/7.25)	0.4 (0.2/2.8)	**<0.001[u]**
WBC, median (q1/q3)	9.47 (7.59/12.07)	9.775 (7.57/13.22)	9.43 (7.61/11.39)	0.155[u]
STONE Score, median (q1/q3)	11 (7/13)	4.5 (3/6)	12 (11/14)	**<0.001[u]**
Age, n (%)				**0.011[rc]**
>50	91 (27.0)	37 (37.0)[sp]	54 (22.8)	AUC (SE): 0.588 (0.034)
≤50	246 (73.0)	63 (63.0)	183 (77.2)[ss]	
CRP, n (%)				**<0.001[rc]**
>0.4	146 (43.3)	63 (63.0)[sp]	83 (35.0)	AUC (SE): 0.668 (0.031)
≤0.4	191 (56.7)	37 (37.0)	154 (65.0)[ss]	
STONE Score, n (%)				**<0.001[rc]**
≤9	104 (30.9)	94 (94.0)[sp]	10 (4.2)	AUC (SE): 0.971 (0.011)
>9	233 (69.1)	6 (6.0)	227 (95.8)[ss]	

[u]Mann Whitney U test (Monte Carlo), [c]Pearson chi-square test (Monte Carlo), [OR]Odds Ratio (%95 confidence interval), [rc]Receiver operating characteristics (ROC) curve analysis (Honley & McNell-Youden index J), AUC: Area under the ROC curve, q1: percentile 25, q1: percentile 75, [A]Significance according to the "patients without stones" group, [B]Significance according to the "patients with stones" group,
Significant values are shown in bold.
BUN: Blood urea nitrogen, CRP: C-reactive protein, WBC: White blood cells, SD: Standard deviation, SE: Standard error, n: Number

Table 2. Odds ratio for age, presence of nausea and vomiting, and Modified STONE Score						
	B	SE	p value	Odds ratio	Odds ratio (95% CI)	
					Lower	Upper
Age (≥50)	1.712	0.459	**<0.001**	5.542	2.253	13.631
Nausea, vomitting	1.921	0.341	**<0.001**	6.830	3.504	13.315
Modified STONE Score	-4.606	0.547	**<0.001**	100.048	34.230	292.418
Dependent variable: presence of stones, prediction rate of patients with stones=96.2, predictions of patients with non-stones=83, overall accuracy: 92.3, p model: <0.001. Multiple Logistic Regression (Method=Enter), CI: Confidence interval, B: Regression coefficients, SE: Standard error						

Alternative diagnoses according to ureteral stone prevalence and MSS categories are shown in Table 3.

While the imaging results were completely normal in 59 (17.5%) of 100 (29.7%) patients who do not have ureteral stones according to CT scans, pathologies other than ureteral stones were detected in 41 (12.2%) patients. Other pathologies include alternative diagnoses such as acute appendicitis, acute cholecystitis, acute pancreatitis, ovarian cyst rupture, renal infarction, gastrointestinal perforation, etc. (Table 4).

Discussion

This study demonstrated the applicability of the MSS in the Turkish population in patients admitted to the emergency department with suspected acute renal colic. Ureteral stones were detected at a rate of 97.4% in the group with a high MSS This result was similar with the rate of 98% found in the study of Kim et al. (16).

History and physical examination findings are very important in patients presenting to the emergency department, but emergency physicians can use scoring systems as a complementary tool. It was showed in our study that the MSS had a high sensitivity in detecting ureteral stones. Patients with a high MSS are more likely to have ureteral stones. For this reason, patients can be diagnosed without the CT, USG or extra consultation. Thus, rapid discharge of the patient from the emergency department can be planned. For this reason, we think that this scoring system can be preferred by emergency physicians and will reduce the workload and additional cost.

In our retrospective study, 1165 patients with suspected acute renal colic were screened and 598 patients had CT scans. CT imaging method was used in 51.3% of the patients in our own clinic. The rate of CT imaging in our clinic was similar to the rate found in the study of Kim et al. (16).

In our study, the prevalence of ureteral stones was 70.3% whereas in the study conducted by Kim et al. (16) in South Korea, the prevalence of ureteral stones was 79%. In Turkey, the prevalence of ureteral stones varies between 49-84% (17-19).

Table 3. Alternative diagnoses in patients according to modified STONE score categories				
	Low risk (n=19)	Moderate risk (n=18)	High risk (n=4)	Total (n=41)
Acute appendicitis	1	-	-	1
Cholelithiasis	2	2	-	4
Newly detected malignancy	2	1	-	3
Acute pyelonephritis	2	2	-	4
Acute cholecystitis	1	1	-	2
Ovarian cyst	1	2	-	3
Enterocolitis	1	-	1	2
Inguinal hernia	-	2	1	3
Ureteropelvic stenosis	-	1	-	1
Renal infarction	-	1	-	1
Ovarian cyst rupture	1	-	-	1
Pelvic inflammatory disease	-	-	1	1
GIS perforation	1	1	-	2
Endometriosis	-	1	-	1
Thoracolumbar spondylosis	1	-	-	1
Acute pancreatitis	-	1	-	2
Angiomyolipoma	1	-	-	1
Paraganglioma	1	-	-	1
Hydatid cyst of the liver	1	-	-	1
Appendicolith	-	1	-	1
Diverticulitis	-	1	1	2
Adrenal adenoma	1	1	-	2
Aortic syndrome	1	-	-	1
Pneumonia	1	-	-	1
n: Number				

The MSS included the variables male sex, pain duration less than six hours, previous ureter stone history, presence of hematuria, and CRP less than 0.5 mg/dL (16). In our study, all these parameters were the same as the other study findings except gender (16,17). Among the patients included in our study, 226 patients (67.1%) were male. While male gender was an important risk factor compared to females in other studies (16,17), although a high rate of male patients was included in our study, the difference was statistically not significant (p=0.07). Since there is no obstetrics and gynecology department in our hospital, female patients in our region often apply to the emergency departments of other hospitals in the region when they are ill. Therefore, the number of male patients could be higher in our hospital.

Table 4. Alternative diagnoses in patients without ureteral stones

	n	%
Patients having stone	237	70.3
Patients not having stone and not being detected any diseases	59	17.5
Patients not having stone but being detected alternative diseases	41	12.2
Cholelithiasis	4	1.2
Pyelonephritis	4	1.2
Inguinal hernia	3	0.9
Ovarian cyst	3	0.9
New malignancy	3	0.9
Diverticulitis	2	0.6
Enterocolitis	2	0.6
Gastrointestinal perforation	2	0.6
Cholecystitis	2	0.6
Adrenal adenoma	2	0.6
Angiomyolipoma	1	0.3
Aortic syndrome	1	0.3
Appendicitis	1	0.3
Appendicolith	1	0.3
Endometriosis	1	0.3
Hydatid cyst of the liver	1	0.3
Ovarian cyst rupture	1	0.3
Pancreatitis	1	0.3
Paraganglioma	1	0.3
Pelvic inflammatory disease	1	0.3
Pneumonia	1	0.3
Renal infarction	1	0.3
Thoracolumbar spondylosis	1	0.3
Ureteropelvic stenosis	1	0.3

Although male gender was a risk factor according to the MSS, it was not a risk factor in our study. This may be a difference seen in our society.

In our study, the prevalence of ureteral stones was 227/233 (97.4%) in the high-risk group, 10/56 (17.8%) in the intermediate-risk group, and 0/48 (0%) in the low-risk group. The prevalence of alternative diagnosis is increasing from the high-risk group to the low- and intermediate-risk group. In the alternative diagnosis group, the prevalence was found to be 39.6% (19/48) for the low-risk group, 32.1% (18/56) for the medium risk group, and 1.7% (4/233) for the high-risk group. These findings also showed similarities as in the study of Kim et al. (16).

We found the alternative diagnosis rate to be 12.1% in patients who applied to our emergency department with the suspicion of acute renal colic. In similar studies, the rate of alternative diagnosis varies between 10% and 22.1% (20-22). The higher rate of alternative diagnosis in other countries compared to our country can be explained by the more widespread use of CT imaging.

As in the study of Kim et al. (16), we determined the optimum cut-off value for MSS as 10, and according to this cut-off value, two groups were designated as MSS positive and MSS-negative. The MSS positive group corresponds to the high-risk group and includes patients with a MSS of 10 or more. The prevalence of ureteral stones in the MSS positive group was 97.4% in our study, while it was 98.0% in the study of Kim et al. (16).

In our study, important alternative diagnoses were found to be 1.7% in the MSS positive group. These diagnoses were diverticulitis, inguinal hernia, enterocolitis and pelvic inflammatory disease. In the study of Kim et al. (16), the rate of significant alternative diagnosis in the MSS positive group was 1.9% which was similar to the result in our study. On the other hand, the rate of significant alternative diagnosis in the MSS negative group was found to be 35.6% in our study. In the study of Kim et al. (16), this rate was 23.5%. Therefore, it can be said that advanced imaging methods are necessary for patients in the MSS negative group.

It is known that acute renal colic pain is more common in young adult men and often recurs (3-5). Therefore, young patients have frequent admissions to the emergency department. There are studies which showed that patients are exposed to high levels of radiation with CT and this increased the risk of cancer, particularly in younger patients compared to the elderly (23). In addition, unnecessary IT requests both increase the length of stay in the emergency department and

cause additional costs. As seen in our study and other studies, MSS positivity largely detects ureteral stones, and it can be said that additional imaging methods other than ultrasound can be abandoned.

In our study, we detected ureteral stones in 67.4% (233/347) of the patients with MSS positive. In the study of Kim et al. (16), this rate was 64.2%. Accordingly, it can be interpreted that using MSS can reduce the use of CT method by 60-70%, and thus reduce the risk of cancer due to radiation.

Study Limitations

Our study has some limitations. The sample size was relatively small and it was a retrospective study. In addition, the generalizability of the findings is limited as it is a single-center study. The results may differ from region to region or country to country due to differences such as geographical conditions, socioeconomic level, eating and drinking habits that may affect the symptom of acute renal colic. Our study was only for a part of the Turkish population. The results of this study should be supported by multicenter studies that can cover all regions of the country or studies covering different countries. Only patients who underwent CT imaging in the MSS evaluation were examined. However, other imaging methods are also frequently used in our country. These limitations should be considered in future research.

Conclusion

With this study, we found that the MSS is quite successful in predicting ureteral stones. By using this score, emergency physicians will safely reduce the overuse of CT, the costs, and the length of stay in the emergency room. We think that when factors such as nausea and/or vomiting are added to this score, its diagnostic value may increase. The sensitivity and specificity of the MSS should be supported by more extensive studies.

Ethics

Ethics Committee Approval: This study was approved by İstanbul Medipol University Noninvasive Clinical Researches Ethics Committee (decision no: 440, date: 15.04.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and/or Medical Practices: B.G., E.E.Ü., Concept: E.E.Ü., Design: B.G., P.A., E.E.Ü., S.K., Data Collection and/or Processing: B.G., P.A., S.K., Analysis and/or Interpretation: B.G., P.A., E.E.Ü., Literature Search: B.G., P.A., E.E.Ü., S.K., Writing: B.G., P.A., S.K.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Bultitude M, Rees J. Management of renal colic. BMJ. 2012;345:e5499.
2. Golzari SE, Soleimanpour H, Rahmani F, Zamani Mehr N, Safari S, Heshmat Y, et al. Therapeutic approaches for renal colic in the emergency department: a review article. Anesthesiol Pain Med. 2014;4:e16222.
3. Agenosov MP, Kagan OF, Kheyfets VK. Features of urolithiasis in patients of advanced and senile age. Adv Gerontol. 2018;31:368-73.
4. D'Costa MR, Pais VM, Rule AD. Leave no stone unturned: defining recurrence in kidney stone formers. Curr Opin Nephrol Hypertens. 2019;28:148-53.
5. Raja AS, Pourjabbar S, Ip IK, Baugh CW, Sodickson AD, O'Leary M, et al. Impact of a Health Information Technology-Enabled Appropriate Use Criterion on Utilization of Emergency Department CT for Renal Colic. AJR Am J Roentgenol. 2019;212:142-5.
6. Romero V, Akpinar H, Assimos DG. Kidney stones: a global picture of prevalence, incidence, and associated risk factors. Rev Urol 2010; 12: pp. e86-96.
7. Watkins S, Bowra J, Sharma P, Holdgate A, Giles A, Campbell L. Validation of emergency physician ultrasound in diagnosing hydronephrosis in ureteric colic. Emerg Med Australas. 2007;19:188-95.
8. Turk C, Petrik A, Sarica K, Seitz C, Skolarikos A, Straub M, et al. EAU Guidelines on Urolithiasis. Eur Urol. 2016;69:475-82.
9. Brisbane W, Bailey MR, Sorensen MD. An overview of kidney stone imaging techniques. Nat Rev Urol. 2016;13:654-62.
10. National Research Council Health risks from exposure to low levels of ionizing radiation: BEIR VII phase 2. Washington, DC: National Academies Press, 2006.
11. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, et al. Solid cancer incidence in atomic bomb survivors: 1958–1998. Radiat Res. 2007;168:1-64.
12. Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet. 2012;380:499-505.
13. Mathews JD, Forsythe AV, Brady Z, Butler MW, Goergen SK, Byrnes GB, et al. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. BMJ. 2013;346:f2360.
14. Berrington de González A, Mahesh M, Kim KP, Bhargavan M, Lewis R, Mettler F, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. Arch Intern Med. 2009;169:2071-7.
15. Moore CL, Bomann S, Daniels B, Luty S, Molinaro A, Singh D, et al. Derivation and validation of a clinical prediction rule for uncomplicated ureteral STONE--the STONE score: retrospective and prospective observational cohort studies. BMJ. 2014; 348: pp. g2191.
16. Kim B, Kim K, Kim J, Jo YH, Lee JH, Hwang JE, et al. External validation of the STONE score and derivation of the modified STONE score. Am J Emerg Med. 2016;34:1567-72.
17. Acar YA, Uysal E. External validation of STONE, modified STONE, and CHOKAI scores for the diagnosis of ureteral stones in the Turkish population. Hong Kong J Emerg Med. 2020; doi: 10.1177/1024907920945476.
18. Rohat A, Kurt E, Şenel Ç. The comparison of two prediction models for ureteral stones: CHOKAI and STONE scores. Am J Emerg Med. 2020. doi: 10.1016/j.ajem.2020.08.099 S0735675720307932
19. Uzun A, Korkut M, Kartal M, Bedel C. Evaluation of modified STONE score in patients presenting to the emergency department with flank pain. Urol Sci. 2020;31:5.

20. Moore CL, Daniels B, Singh D, Luty S, Molinaro A. Prevalence and clinical importance of alternative causes of symptoms using a renal colic computed tomography protocol in patients with flank or back pain and absence of pyuria. Acad Emerg Med. 2013;20:470-8.
21. Samim M, Goss S, Luty S, Weinreb J, Moore C. Incidental findings on CT for suspected renal colic in emergency department patients: prevalence and types in 5,383 consecutive examinations. J Am Coll Radiol. 2015;12:63-9.
22. Lokken RP, Sadow CA, Silverman SGS. Diagnostic yield of CT urography in the evaluation of young adults with hematuria. AJR Am J Roentgenol. 2012;198:609-15.
23. Sodickson A, Baeyens PF, Andriole KP, Prevedello LM, Nawfel RD, Hanson R, et al. Recurrent CT, cumulative radiation exposure, and associated radiation-induced cancer risks from CT of adults. Radiology. 2009;251:175-84.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2021.93270
Eurasian J Emerg Med. 2022;21(2): 146-51

Emergency Physicians' Point of Care Ultrasonography (POCUS) Competency Assessment for the Diagnosis of Acute Appendicitis in Pediatric Cases

Hasan Atalar[1], Mustafa Keşaplı[2], Ömer Faruk Karakoyun[3], Adeviyye Karaca[2]

[1]Clinic of Emergency Medicine, Bucak State Hospital, Burdur, Turkey
[2]Clinic of Emergency Medicine, Antalya Training and Research Hospital, University of Health Sciences Turkey, Antalya, Turkey
[3]Department of Emergency Medicine, Sıtkı Koçman University Training and Research Hospital, Muğla, Turkey

Abstract

Aim: To evaluate the accuracy of emergency physicians performed point-of-care ultrasonography (EP-POCUS) in diagnosing acute appendicitis (AA) in the pediatric age group who had abdominal pain and compare sonographic findings with those of radiologists.

Materials and Methods: One hundred twenty-three children who had abdominal pain were included in the study. EP-POCUS and radiology department ultrasonography (RADUS) performed on each case. Sonographic findings [non-compressible bowel loops, target sign, edema in the surrounding tissue, appendix diameter, peri-appendiceal abscess, appendicitis positivity (a non-compressible and non-peristaltic blind ending tubular structure >6 mm) and presence of mesenteric lymphadenitis] of the EP-POCUS and RADUS were recorded seperately and compared to evaluate accuracy of the EP-POCUS and RADUS. Definitive diagnoses were determined by pathological evaluation of appendectomy specimens.

Results: Thirty-six (29.2%) patients were diagnosed AA and hospitalized by the surgeon, 30 (24.3%) of which were confirmed pathologically. According to pathological diagnose, the EP-POCUS's sensitivity was 73.3%, specificity was 89.2%, the RADUS's sensitivity was 76.7%, the specificity was 96.8% and significantly consistent with in diagnosing AA (Kappa coefficient: 0.64, $p<0.005$). EP-POCUS accuracy in AA diagnosis did not differ between age groups.

Conclusion: EP-POCUS on pediatric patients acts as an auxiliary and useful approach in AA diagnosis. Training and experience may increase the accuracy rates.

Keywords: Acute appendicitis, bedside ultrasonography, pediatrics, point-of-care ultrasonography

Introduction

Among the causes of abdominal pain in childhood, the most common reason that requires urgent surgery is acute appendicitis (AA) (1-3). The diagnosis is relatively easy in adolescents and adults but somewhat more difficult in children. Lack of typical symptoms and communication skills, may lead to diagnosis delays in childhood appendicitis and consequently increased mortality and morbidity (2).

The difficulties experienced in physical examination in children make it necessary to use additional diagnostic methods. Although the gold standard diagnostic method is computed tomography (CT) (1), ultrasonography (USG) is preferred in pediatric patients to prevent exposure to contrast agents, large amount of radiation, and need to ensure immobility for a long time, (USG) is a cost-effective first-line diagnostic tool with no radiation risk, It can be performed bedside easily in crowded emergency settings. Thin subcutaneous adipose tissue in children is an advantage for application of (USG) not only to diagnose AA but also other pathologies causing abdominal pain such as acute mesenteric lymphadenitis, intussusception, acute cholecystitis, gynecological and urinary pathologies in chidhood.

Corresponding Author: Adeviyye Karaca, M.D., Clinic of Emergency Medicine, Antalya Training and Research Hospital, University of Health Sciences Turkey, Antalya, Turkey
E-mail: ade.aksoy@gmail.com ORCID ID: orcid.org/0000-0002-5338-1826

Received: 22.09.2021
Accepted: 27.12.2021

Cite this article as: Atalar H, Keşaplı M, Karakoyun ÖF, Karaca A. Emergency Physicians' Point of Care Ultrasonography (POCUS) Competency Assessment for the Diagnosis of Acute Appendicitis in Pediatric Cases. Eurasian J Emerg Med. 2022;21(2):146-51.

Emergency physicians commonly use Point-of-Care Ultrasonography (POCUS) technique that focuses on the highest probability areas with high sensitivity and specificity (2). However, no comparative study includes ultrasonographic signs of AA and compares the signs between radiologists and emergency physicians (EP). Therefore, despite several literature reviews on the efficacy of EP performed Point-of-Care Ultrasonography (EP-POCUS) for AA in the pediatric emergency department (ED), controversy remains. There is a good deal of practices and centers where EPs are routinely performing this scan. This study aimed to evaluate the competence of EP-POCUS in diagnosing AA and compare the sonographic signs with that of abdominal USG performed by a radiologist (RADUS) in the diagnosis of AA in the 0-18 age group who admitted to the Pediatric ED.

Materials and Methods

Study Design

This was a prospective observational study. The ethics committee approval was obtained from Antalya Training and Research Hospital Clinical Research Ethics Committee (decision no: 2/008, date: 24.01.2019). The study did not interfere with the patients' therapeutic and diagnostic procedures, and the patients were not exposed to any risks. The pediatric patients with abdominal pain and physical examination findings resembling AA were studied. Written consent was obtained from the parents of the patients. EP-POCUS was performed on each case by the EP who managed the patient. A physician from the Radiology department also performed abdominal ultrasonofraphy (RADUS) on the same cases. Sonographic findings of the EP-POCUS and RADUS were recorded separately for each patient and compared to evaluate accuracy of the EP-POCUS with regard to RADUS. The sensitivity and specificity of EP-POCUS and RADUS were determined by comparing the diagnoses with pathologic biopsy results.

Study Population

The study group consisted of patients with abdominal pain and physical examination findings resembling AA under the age of 18 who admitted to the Yellow Triage Zone of Antalya Training and Research Hospital Pediatric Emergency Service between the dates 15.11.2018 and 01.04.2019. Unstable patients, patients with trauma history and findings, and those who underwent abdominal imaging at other medical centers before referral to the pediatric ED were excluded from the study. Also, patients without a pre-diagnosis of AA were excluded. The study group was classified into three age groups as preschool period (0-5 years old), school period (6-12 years old) and adolescence (13-18 years old) to simplify the ages.

The estimated sample size was calculated based on other studies using POCUS for similar indications. After sample size calculation, it was estimated that at least 123 volunteers were required to detect statistically significant differences, admitting a type I error rate of 0.05 and a power of 80%.

The physicians who performed POCUS received 16-hour training (8 hours of theoretical course and 8 hours of practicals) on implementation of POCUS to detect acute appendicitis. The training was organized by the Emergency Medicine Physicians Association of Turkey (EPAT). Emergency physicians and radiologists were informed about the study in advance.

Of the cases taken into consideration; age, gender, symptoms, vital signs, physical examination findings, leukocyte count, EP-POCUS, and RADUS findings [non-compressible bowel loops, target sign, edema in the surrounding tissues, appendix diameter, peri-appendiceal abscess, appendicitis positivity (a non-compressible and non-peristaltic blind ending tubular structure >6 mm), presence of mesenteric lymphadenitis], discharge, operation, and pathological results were recorded.

Patients with suspected AA findings, 0-18 years of age and performed RADUS were included in the study.

Study Protocol (EP-POCUS Technique)

EP-POCUS measurements were made by Mindray DC-T6 US device and RADUS measurements by the radiologist with Toshiba SSA-660A ultrasound device. EPs and radiologists used the same probe, a 7.5-MHz linear probe, and the same compression technique.

First of all, the EP performed clinical questioning and physical examination for abdominal pain, and EP-POCUS was applied before the diagnostic tests. Then, the same performers noted the sonographic findings into the data collection form. Finally, RADUS was performed with using the same technique.

The EP-POCUS was performed in a standardized manner. If the patient can localize the pain well, the imaging protocol started from that localization. In other conditions, the POCUS performer using the graded compression method started at the umbilicus level, in the transverse plane with a linear probe. The probe was moved towards the ascending colon to the lateral abdominal wall. When the ascending colon was identified, follow the ascending colon's lateral edge by moving the probe inferiorly until the cecum's end. The probe was moved medially, and the iliac artery, vein, and psoas muscle were identified. The pelvis and umbilicus were scanned by seeing the psoas muscle and iliac vessels at the same image plane. Afterward, the probe was given a sagittal position to sagittal scanning, and the long axial imaging of the end of the cecum was identified. During the scanning, the cecum was compressed with probe against the psoas muscle.

The physician tried to visualize the appendix to evaluate the non-compressible bowel loops, target sign, edema in the surrounding tissue, appendix diameter, peri-appendiceal abscess, appendicitis positivity (a non-compressible and non-peristaltic blind ending tubular structure >6 mm) and presence of mesenteric lymphadenitis. The EP-POCUS findings were recorded in the study form. The positive indications for AA diagnosis were appendiceal diameter above 6 millimeters and nonperistaltic and noncompressible tubular structures. Absence of target sign, peri-appendiceal abscess, and secondary inflammatory findings, such as mesenteric lymphadenitis, non-compressible bowel loops, and edema in the surrounding tissue and appendiceal diameter equal or under 6 millimeters, or inability to visualize appendix were considered as unfavorable for AA. The consulting pediatric surgeon made the clinical management decision of the patient.

Radiologists on duty performed RADUS for all study patients. None of the patients had CT scan.

A blinded physician reviewed the EP-POCUS and RADUS findings and pathology reports. The parents of the discharged patients were called by the physician three weeks later after the examinations were performed to determine that they had undergone appendicitis surgery later.

The exact diagnosis of AA was made according to pathology results. In contrast, exact no appendicitis diagnosis was made upon negative pathology reports or recuperating the patients' symptoms during three weeks follow-up time.

Measures

This study aimed to evaluate the competence of EP-POCUS in diagnosing AA and compare the sonographic signs with that of RADUS in the diagnosis of AA in the 0-18 age group who admitted to the Pediatric ED.

The primary outcome measures were the consistency between EP-POCUS and RADUS findings for the diagnosis of AA. Besides, the diagnostic value, sensitivity and specificity of EP-POCUS for AA in the pediatric ED were evaluated in the study.

Statistical Analysis

The analyses were performed using SPSS for Windows 22 package (IBM Corp., Armonk, NY, USA) program. Descriptive statistics were shown as mean ± standard deviation for continuous and discrete numerical variables, number of cases, and (%) for categorical variables. Chi-square test was used for categorical variables. False positive, false negative, sensitivity, specificity, positive predictive value (PPD), negative predictive value (NPD), for sonographic evaluations and kappa coefficient for compatibility were calculated. Although there is no consensus on how to decide borders and ranges and most researches divide Kappa coefficient into five groups, we divided the range into three groups acoording to the Fleiss' kappa statistic which is a well-known index for assessing the reliability of agreement between raters." Compatibility was considered perfect for Kappa coefficients greater than 0.75, moderate for the values between 0.75 to 0.40, and poor for the values less than 0.40. P values less than 0.05 was accepted to show statistical significance.

Results

In the study, five different EPs performed POCUS in the ED and four different radiologists performed RADUS. Thirty-nine (29.3%) of the patients were hospitalized, 87 (70.7%) of them were discharged from the ED. One patient was discharged from hospital without having an operation. Thirty-five patients underwent an operation, and AA was confirmed in 30 of them by pathological evaluation. Laparotomy was negative in five patients, in which EP-POCUS and RADUS were negative in different three of them. Sixty-nine (56.1%) of the study patients were male, and 54 (43.9%) were female. Of the patients included, seven (5.7%) were under the age of 6, 60 (48.8%) were between the ages of 6-12, 56 (45.5%) were between the ages of 12-18 (Table 1).

The false-positive results obtained by emergency physicians were mostly found in evaluation of the appendix diameter and diagnose of the presence of appendicitis. The highest value for false negativity was determined as the presence of mesenteric lymphadenitis. False positivity, false negativity, and kappa coefficient of EP-POCUS findings of the patients included in the study are shown in Table 2. When EP-POCUS findings were evaluated individually, the highest consistency was evaluating the edema in the surrounding tissue (kappa: 0.88). When EPs were evaluated to determine the presence of AA with POCUS, the false negativity value was 8, the false positivity value was 9, and the kappa coefficient was 0.64.

Table 1. Demographic characteristics of the patients

Variables	n	%
Gender		
Female	54	43.9
Male	69	56.1
Ages in years		
0-6	7	5.7
6-12	60	48.8
12-18	56	45.5
Total	123	100.0

n: Number of patients

According to the pathological reports, EP-POCUS's sensitivity was 73.3% and specificity was 89.2%. Their sensitivity in detecting the presence of appendicitis was 80.8%, their specificity was 88.7%, PPD was 65.6%, and NPD was 94.5%. When the findings of EP-POCUS were examined one by one, it was found that the highest specificity was the edema in the circumference of the intestines (100%), and then the non-compressible bowel loops (90.6%) (Table 2). According to the pathological results, the RADUS evaluation's sensitivity was 76.7%, and the specificity was 96.8% (Table 3). There was a moderate consistency between EP-POCUS and RADUS results [Kappa coefficient: 0.64, p=0.001 95% confidence interval (CI)].

Although four (3.2%) of the discharged patients re-applied to different hospitals, no appendectomy was performed. In the EP-POCUS evaluation, 24 of the 36 patients hospitalized were evaluated in favor of AA.

Eight of the 91 discharged patients were diagnosed with AA in the EP-POCUS evaluation.

According to pathology results, there was no significant difference between the age groups and the EP-POCUS evaluation (p=0.18).

Discussion

In the pediatric age group, evaluation of abdominal pain, a frequent reason for admission in the ED, is difficult due to communication limitations, anamnesis, and physical examination. Differential diagnosis of abdominal pain, USG is preferred primarily because fast, easy to apply, and has no radiation effect. In the literature, there are many studies on the diagnostic confirmation effectiveness of EP-POCUS performed in the ED.

In the meta-analysis made by Lee and Yun (4), in 2018, POCUS evaluation was more successful in pediatric patients than in adults in diagnosing AA. Less subcutaneous adipose tissue in the pediatric patient group was found to facilitate imaging of the appendix compared to adults. However, in the study of Nicole et al. (5), POCUS was found inconsistent in the pediatric patient group according to the RADUS evaluation. In studies evaluating the diagnosis of AA in the current literature, the sensitivity of POCUS administration was expressed in a wide range of 40% to 94%.

In a retrospective study by Fox et al. (6) in 2007, EPs' competencies to diagnose AA with POCUS were evaluated. In this study, EP-POCUS was compared with RADUS. As a gold standard, RADUS, abdominal CT, and pathology reports were accepted. In this study, which was conducted on 155 cases, the EP-POCUS assessment's sensitivity was 39%, and the specificity was 90%. In our study, the EP-POCUS's sensitivity was 66%, and the specificity was 91% for the patients who underwent an appendectomy.

In the study conducted by Elikashvili et al. (7) in 2014, the effectiveness of EP-POCUS for diagnosing AA was evaluated. EPs who will make the evaluation were given a 30-minute vocal and 30-minute practical training, and a standard was established in terms of findings. Findings were compared with

Table 2. Test characteristics and concordance of EP-POCUS and RADUS findings (n=123)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Kappa coefficient	p*
Edema in surrounding tissue	80.0	100.0	100.0	98.3	0.880	<0.001
Non-compressible appendix	81.5	90.6	71.0	94.6	0.685	<0.001
Appendix diameter >6 mm	81.5	89.6	68.8	94.5	0.666	<0.001
Presence of appendicitis	80.8	88.7	65.6	94.5	0.640	0.001
Any ultrasonography finding considering AA	74.0	87.7	80.4	83.1	0.625	<0.001

*Chi-square test.
EP-POCUS: Point-of-care ultrasonography performed by emergency physician, RADUS: Abdominal ultrasonography performed by radiologist, PPV: Positive predictive value, NPV: Negative predictive value, AA: Acute appendicitis, n: Number of patients

Table 3. Accuracy of EP-POCUS and RADUS according to pathology reports of the patients (n=123)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Kappa coefficient/p*
EP-POCUS	73.3	89.2	68.8	91.2	0.612/<0.001
RADUS	76.7	96.8	88.5	92.8	0.769/<0.001

*Chi-square test.
EP-POCUS: Point-of-care ultrasonography performed by emergency physician, RADUS: Abdominal ultrasonography performed by radiologist, PPV: Positive predictive value, NPV: Negative predictive value, n: Number of patients

EP-POCUS, RADUS, and CT performed in the ED. While in the study conducted by Elikashvili et al. (7), RADUS, and CT were the gold standard, appendectomy and RADUS evaluations were accepted in our study. As a result of the study; In EP-POCUS evaluation, sensitivity was 60%, and specificity was 94%, while in RADUS evaluation, sensitivity was 62.5% and specificity was 99.3%. In our study, sensitivity was 66%, and specificity was 91% in the EP-POCUS evaluation, while 77% and specificity were 100% in the RADUS evaluation. Compared to the patients who underwent an appendectomy in our study, the sensitivity and specificity of patients were found to be close to each other. It was emphasized by Elikashvili et al. (7) that the experience of the practitioner was the most critical criterion affecting the outcome of the study. Although the practitioners received standard basic ultrasonography training in our study, no data was provided about their experience. However, it was concluded that the sensitivity and specificity values depending on the experience could change positively.

In the study of Sivitz et al. (8), in 2014, patients diagnosed with AA and who underwent RADUS were evaluated. Before the study, EPs were verbally and practically given POCUS training on AA. The EP-POCUS, and the RADUS was compared. In the study, which included 264 pediatric patients, the EP-POCUS's sensitivity at the bedside was 85%, and the specificity was 93%. In our study, the sensitivity was found to be 66% and was lower than this study. The reason for this is that, in our study, EPs who performed POCUS received a total of 16 hours of theoretical and practical training, at a basic and advanced level, and did not have specific training for the diagnosis of AA.

In the prospective study conducted by Doniger et al. (9) in 2016, 40 patients admitted due to abdominal pain between the ages of 2 and 18 were compared with the confirmation of the diagnosis of AA by comparing their POCUS and other radiological methods. The sensitivity of 93.8% and 85.7% of EP-POCUS were determined. In RADUS evaluation, sensitivity was 81.25%, while specificity was 100%. As a result of this study, it was suggested that POCUS evaluation has an acceptable diagnostic value. However, the patients' physical characteristics may create obstacles in the procedure (9). In our study, the sensitivity of EP-POCUS was low compared to this study, and we did not make an additional evaluation in terms of personal physical properties.

As a result of our study findings, the diagnosis was moderately compatible (kappa=0.64). To the best of our knowledge, there is no comparison of ultrasonography findings between EP-POCUS and RADUS in pediatric patients was found in the literature. Since appendicitis ultrasonography findings were similar in pediatric and adult patients, studies for adult patients in the literature were reviewed for compliance. In the study conducted by Gungor et al. (10). In 2017, on 264 adult patients, EP-POCUS appendix circumference was detected in 69% of patients. Another data in the same study, EP-POCUS sensitivity and specificity were 92.3% and 95.8%, while RADUS sensitivity and specificity were 76.9% and 97.8%, respectively. In diagnosing AA, the kappa coefficient between EP-POCUS and RADUS was 0.66 with moderate compliance. In our study, the kappa coefficient between EP-POCUS and RADUS in AA diagnosis was moderately compatible with 0.64. It was similar to the study on these adults in the literature (Table 2).

Study Limitations

The nature of POCUS is highly operatory dependent. Therefore, the accuracy of POCUS may alter regard in the performer's experience.

The study was a single centre study with five EPs and four radiologists involved and may not be externally valid to other centres.

Doctors performing POCUS were not blinded to the patients' history and physical examination, which may have influenced their interpretation of the ultrasound.

Anatomical variation of the appendix (appendix showing various variations, especially retrocecal), fat mass of the patient and excessive amount of intestinal gas in the abdomen may affect to the interpretation of the ultrasound.

The uncontrolled adequacy of ultrasonographic images in both EP-POCUS and RADUS groups (physicians decided by themselves).

The "inter-rater agreement" between five EPs and four radiologist prior the study with a smaller sample size different from study group did not tested.

Conclusion

When the data of this study and similar studies in the literature are analyzed, it was seen that the bedside EP-POCUS had an auxiliary and accelerating effect on early diagnosis in pediatric patients. The fact that the physician is trained and experienced in this regard will increase the diagnosis's success rate.

Ethics

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Antalya Training and Research Hospital, decision no: 2/008, date: 24.01.2019).

Informed Consent: Informed consent was obtained from all the parents of the participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and/or Medical Practices: H.A., Ö.F.K., Concept: H.A., M.K., Ö.F.K., Design: H.A., M.K., Data Collection and/or Processing: H.A., Ö.F.K., Analysis and/or Interpretation: M.K., A.K., Literature Search: Ö.F.K., A.K., Writing: H.A., A.K.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Wu CC, Khorashadi L, Abbott GF, Gilman MD. Common blind spots on chest CT: where are they all hiding? Part 1-airways, lungs, and pleura. AJR Am J Roentgenol. 2013;201:W533-8.
2. Zhang H, Liao M, Chen J, Zhu D, Byanju S. Ultrasound, computed tomography or magnetic resonance imaging - which is preferred for acute appendicitis in children? A Meta-analysis. Pediatr Radiol. 2017;47:186-96.
3. Rebecca M. Rentea, Shawn D. St. Peter, Charles L. Snyder. Pediatric appendicitis: state of the art review. Pediatr Surg Int. 2016. doi: 10.1007/s00383-016-3990-2
4. Lee SH, Yun SJ. Diagnostic performance of emergency physician-performed point-of-care ultrasonography for acute appendicitis: A meta-analysis. Am J Emerg Med. 2019;37:696-70.
5. Nicole M, Desjardins MP, Gravel J. Bedside sonography performed by emergency physicians to detect appendicitis in children. Acad Emerg Med. 2018;25:1035-41.
6. Fox JC, Hunt MJ, Zlidenny AM, Oshita MH, Barajas G, Langdorf MI. Retrospective analysis of emergency department ultrasound for acute appendicitis. Cal J Emerg Med. 2007;8:41-5.
7. Elikashvili I, Tay ET, Tsung JW. The effect of point-of-care ultrasonography on emergency department length of stay and computed tomography utilization in children with suspected appendicitis. Acad Emerg Med. 2014;21:163-70.
8. Sivitz AB, Cohen SG, Tejani C. Evaluation of acute appendicitis by pediatric emergency physician sonography. Ann EmergMedic. 2014;64:358-64.
9. Doniger SJ, Salmon M, Lewiss RE. Point-of-care ultrasonography for the rapid diagnosis of intussusception: a case series. Pediatric Emerg Care. 2016;32:340-2.
10. Gungor F, Kilic T, Akyol KC, Ayaz G, Cengiz Çakır U, Akçimen M, et al. Diagnostic value and effect of bedside ultrasound in acute appendicitis in the emergency department. Acad Emerg Med. 2017;24:578-86.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2020.44265
Case Report
Eurasian J Emerg Med. 2022;21(2): 152-5

A Rare Cause of Intraabdominal Haemoraggy Ethiology: Retroperitoneal Haemoragic Cyst

Mehmet Buğra Bozan[1], Fatih Mehmet Yazar[1], Özlem Güler[2], Ömer Faruk Boran[3], Ayşe Azak Bozan[4]

[1]Department of Surgery, Kahramanmaraş Sütçü İmam University Faculty of Medicine, Kahramanmaraş, Turkey
[2]Department of Emergency Medicine, Kahramanmaraş Sütçü İmam University Faculty of Medicine, Kahramanmaraş, Turkey
[3]Department of Anesthesiology and Reanimation, Kahramanmaraş Sütçü İmam University Faculty of Medicine, Kahramanmaraş, Turkey
[4]Department of Anesthesiology and Reanimation, Kahramanmaraş Necip Fazıl State Hospital, Kahramanmaraş, Turkey

Abstract

Primary retroperitoneal cysts are rare benign lesions. Generally, these lesions originates from lymphatic system hipoplasia or pelvic or retroperitoneal operations. Although it is usually asymptomatic, they can cause symptoms as hipotension, tachicardia or even shock due to intracystic haemorhaggy, gas retantion or hydronephrosis due to compression of adjacent organs. Definitive diagnosis is diffucult before surgery. However, diagnosis can be estimated by direct graphy, computed tomography, ultrasound and other techniques. Conservative treatments, percutaneous drainage, marsupialization, open or laparoscopic cyst excision are the treatment options. In this case report, we present a case of retroperitoneal hemorrhagic cyst which was opened to the abdomen causing acute abdomen.

Keywords: Acute abdomen, retroperitoneal cyst, intraabdominal hemorrhage

Introduction

Retroperitoneal cysts are rare, usually asymptomatic, slow growing, abdominal lesions. Although it is often observed as an asymptomatic mass, it can be seen with symptoms such as cyst exerting pressure on surrounding tissues (such as hydronephrosis, gaseous distension) and intracystic hemorrhage (1,2).

In this case report, we presented the patient who was admitted with acute abdomen due to rupture of intracystic hemorrhage into the abdomen.

Case Report

A 45-year-old woman who had abdominal pain for about two days was admitted to the emergency department. The patient also had complaints of palpitation and fatigue. Physical examination revealed widespread tenderness and rebound in the abdomen. No pathology was found in other system examinations. The patient's hemoglobin level and hematocrit level were 8 gr/L and 23.7%. No other pathological findings were observed. No pathologies were observed on abdominal X-ray. In emergency abdominal computed tomography (CT), on the left, a lesion with intra-heterogeneous character, approximately 10.5x8.5 cm in size, was observed in retroperitoneal space, and a cystic mass was observed in right ovarian, approximately 4x5 cm in size (Figures 1-3). In the follow-up of the patient who was hospitalized by the obstetrics clinic, tachycardia and hypotension and shock clinic was observed despite blood and fresh frozen plasma. An emergent surgery was performed after observing hypovolemic shock. A single dose of prophylactic cefazolin 1 g was administered intravenously prior to the operation, then the abdomen was entered with pfannenstiel incision. Widespread hemorrhagic fluid was observed in the abdomen. Following the observation that the bleeding was not originated from the ovarian mass, the general surgery department was included to the operation. Abdomen was entered with a midline incision on upper and lower abdomen. In the exploration conducted, intraabdominal hemorrhagic fluid was observed. After aspiration of the fluid, when the exploration continued, a bleeding area of approximately 5 cm from the retroperitoneal area was observed

Corresponding Author: Asst. Prof. Mehmet Buğra Bozan, Ph.D., Department of Surgery, Kahramanmaraş Sütçü İmam University Faculty of Medicine, Kahramanmaraş, Turkey
E-mail: bbozan@yahoo.com ORCID ID: orcid.org/0000-0001-5573-2645

Received: 03.11.2019
Accepted: 13.05.2020

Cite this article as: Bozan MB, Yazar FM, Güler Ö, Boran ÖF, Azak Bozan A. A Rare Cause of Intraabdominal Haemoraggy Ethiology: Retroperitoneal Haemoragic Cyst. Eurasian J Emerg Med. 2022;21(2):152-5.

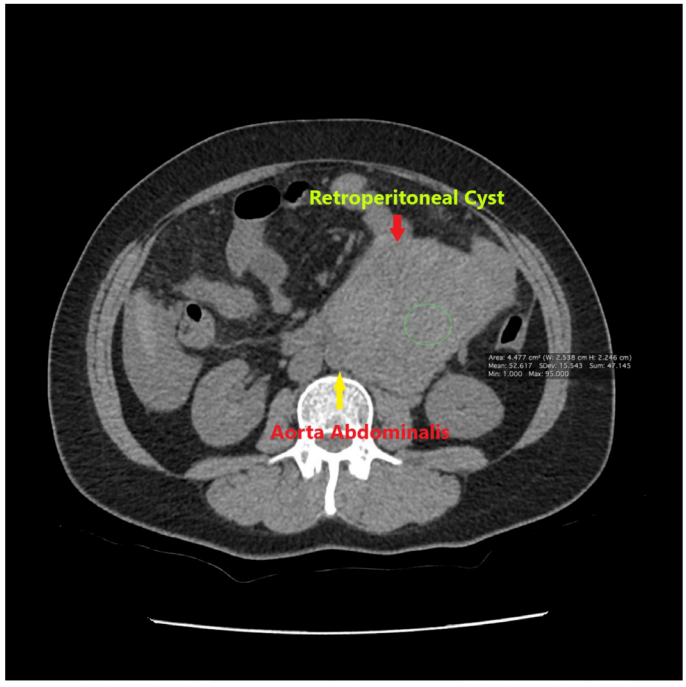

Figure 1. Preoperative coronal computerized tomographic view of the haemoragic cyst

just below the treitz ligament. No aneurysmatic dilatation of aorta was observed. Bleeding was observed in the form of leakage (Figures 4 and 5). Surgicel was applied for homeostasis, and cyst was excised. The operation was terminated. With no complaints and complications in the postoperative period, the patient was discharged.

Discussion

Etiology of nontraumatic retroperitoneal hemorrhages involves an aneurysmatic dilatation of retroperitoneal vessels. Hemorrhages in retroperitoneal vessels without aneurysmatic dilatation are more rare pathologies.

Retroperitoneal cysts are one of the rare pathologies (estimated and expected incidence rates range from 1/5,750 to 1/250,000) (3). As in our case, primary retroperitoneal cystic lesions are benign lesions that do not show any association with other organs or other retroperitoneal structures (1). They are usually formed due to hypoplasia of the congenital lymphatic system, or pelvic or retroperitoneal operations (2). Our case had no known history of pelvic or retroperitoneal operation.

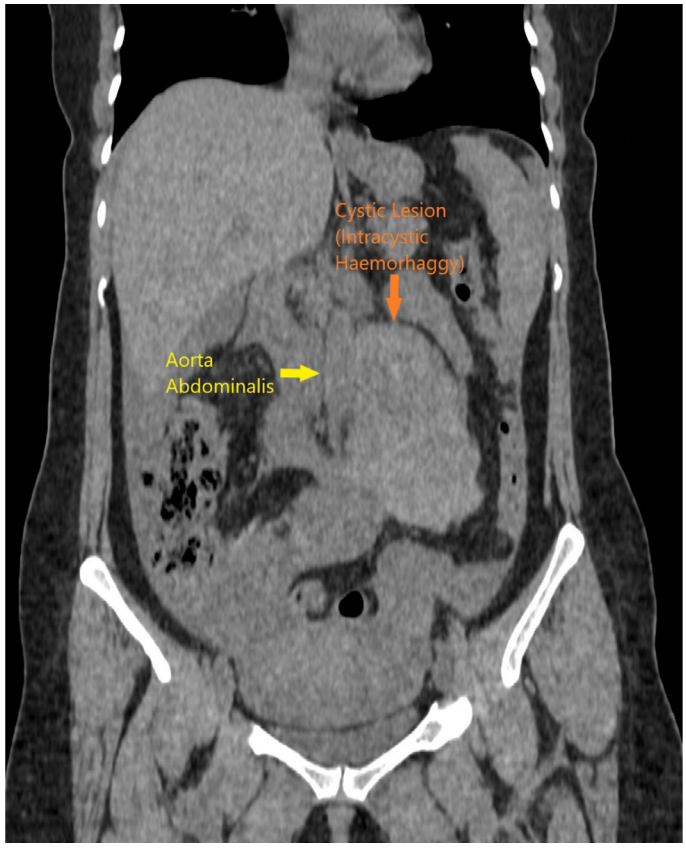

Figure 2. Preoperative sagital computerized tomographic view of the haemoragic cyst

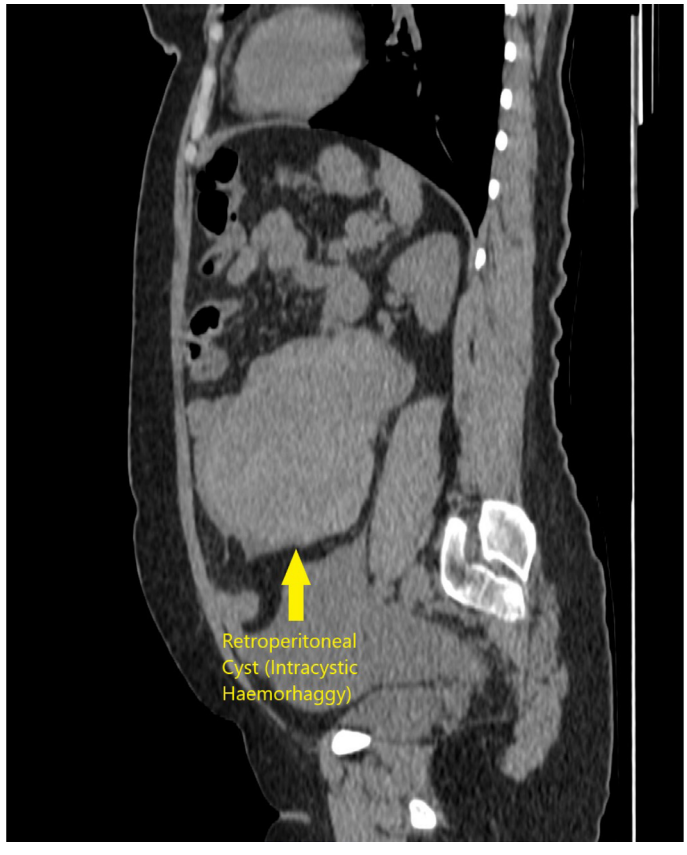

Figure 3. Preoperative axial computerized tomographic view of the haemoragic cyst

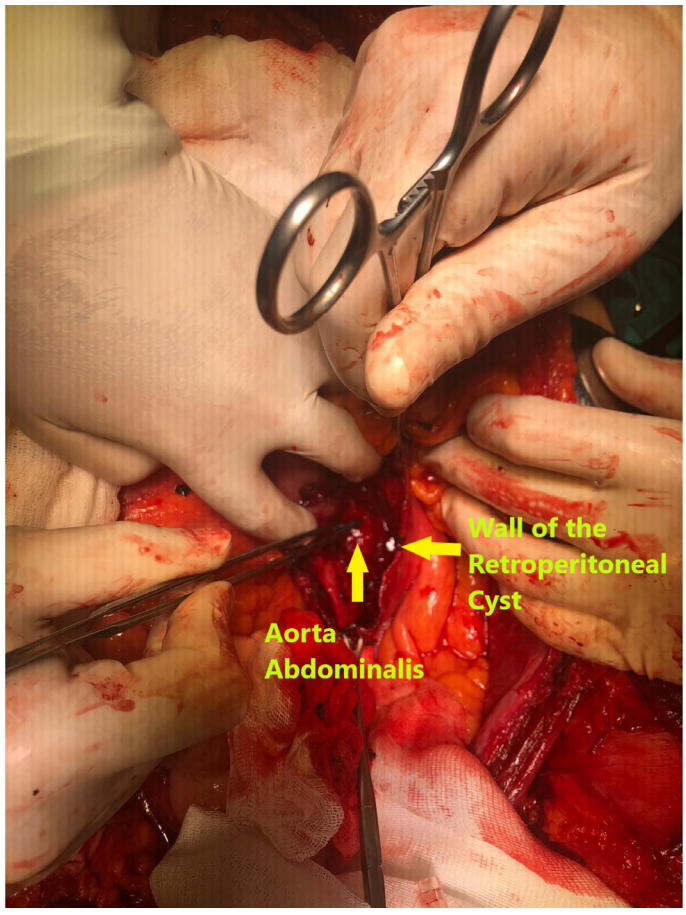

Figure 4. Intraoperative view of the ruptured haemoragic cyst

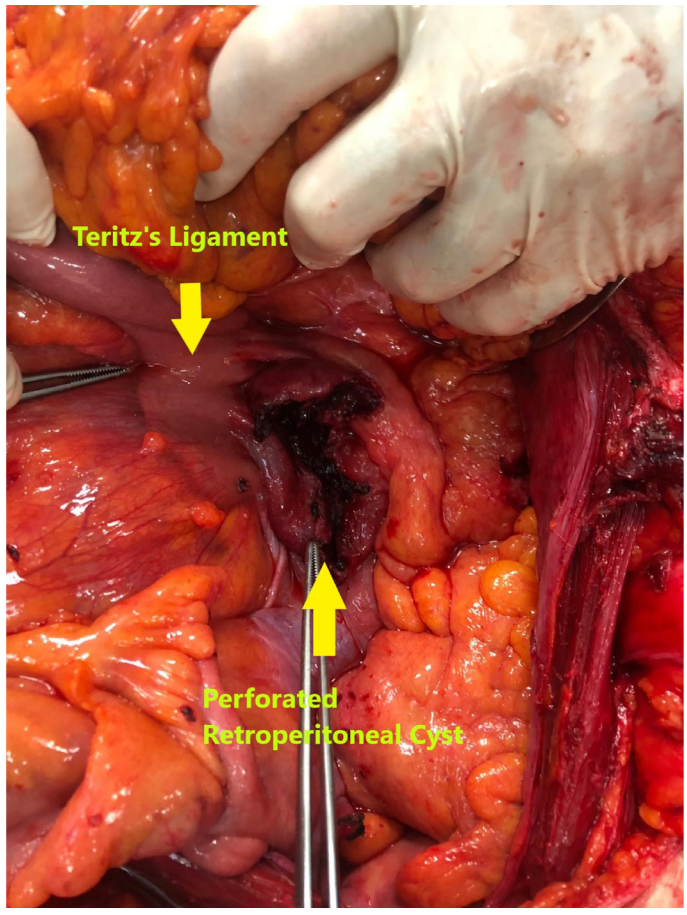

Figure 5. Intraoperative view of the ruptured haemoragic cyst

In the early stage, most cysts are asymptomatic; this is due to the anatomically deep and large cavities, because of the anatomic structure of the retroperitoneal space. At the same time, retroperitoneal lymphatic cysts grow slowly and do not show invasion. However, if the cyst grows too large, the infection may cause some symptoms such as intracystic hemorrhage, gaseous distension as a result of pressure exerted on surrounding tissues, and hydronephrosis as in our case (2). In our case, the cyst has bleeded into itself, and then it was perforated, causing intra-abdominal hemorrhage.

Sometimes painless mass can be palpated in patients (4). It is easily misdiagnosed, and should be distinguished by other intra-abdominal cysts (liver cysts, renal cysts, pancreatic cysts, cystic tumor lesions, cystic teratoma and ovarian cysts as in our case) (5,6). Our patient's initial diagnosis was ovarian cyst, for this reason she was firstly operated by gynecology department. After whole examination and determination of retroperitoneal cyst haemorragy our General Surgery Department was included into the operation.

Definite preoperative diagnosis is difficult (2). However, it can be estimated by direct radiography, CT, ultrasound and other techniques (2). In our case, a lesion was observed in retroperitoneal space in CT, adjacent to the aorta, filled with hemorrhagic fluid in the cyst.

Narrow and deep retroperitoneal space makes surgery difficult, therefore, open surgery is usually the first choice. However, laparoscopic techniques may also be preferred (7). Our case was operated following hemorrhagic shock, and the patient underwent cystectomy with open surgery. If cyst have pressure symptoms, different techniques such as conservative follow-up, percutaneous catheter drainage with or without sclerotherapy and internal marsupialization can be used (2). However, recurrence rates are 13% in the 6-month follow-up after the first successful drainage (8).

In conclusion, in non-traumatic hemorrhage cases in emergency service applications, gynecological pathologies and aneurysmatic dilatations of vascular structures are common pathologies. However, secondary hemorrhage to retroperitoneal cyst hemorrhage, which is a rare cause, should also be considered among etiologic factors.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.B.B., F.M.Y., Ö.G., Ö.F.B., A.A.B., Concept: M.B.B., F.M.Y., A.A.B., Design: M.B.B., Ö.G., Ö.A.B., Data Collection or Processing: M.B.B., A.A.B., Analysis or Interpretation: F.M.Y., Ö.G., Ö.F.B., Literature Search: M.B.B, Ö.F.B., A.A.B., Writing: M.B.B., F.M.Y., A.A.B.

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

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Jha AK, Shrestha S, Sharma S. Idiopathic retroperitoneal cyst in an adult male. Urol Ann. 2017;9:272-4.
2. Wang Y, Chen C, Zhang C, Qin C, Song N. Extraperitoneal laparascopic resection for retropertioneal lymphatic cysts: initial experience. BMC Urol. 2017;17:101.
3. Guile M, Fagan M, Simopolous A, Ellerkman M. Retroperitoneal cyst of mullerian origin: A case report and review of literature. J Pelvic Med Surg. 2007;13:149-52.
4. Martin-Perez E, Tejedor D, Brime R, Larranaga E. Cystic lymphangioma of the lesser omentum in an adult. Am J Surg. 2010;199:e20-2.
5. Dong B, Zhou H, Zhang J, Wang Y, Fu Y. Diagnosis and treatment of retroperitoneal bronchogenic cysts: a case report. Oncol Lett. 2014;7:2157-9.
6. Thaler M, Achatz W, Liebensteiner M, Nehoda H, Bach CM. Retroperitoneal lymphatic cyst formation after anterior lumbar interbody fusion: a report of 3 cases. J Spinal Disord Tech. 2010;23:146-50.
7. Ahn KS, Han HS, Yoon YS, Kim HH, Lee TS, Kang SB, et al. Laparoscopic resection of nonadrenal retroperitoneal tumors. Arch Surg. 2011;146:162-7.
8. Kim JK, Jeong YY, Kim YH, Kim YC, Kang HK, Choi HS. Postoperative pelvic lymphocele: treatment with simple percutaneous catheter drainage. Radiology. 1999;212:390-4.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2020.79037
Letter to the Editor
Eurasian J Emerg Med. 2022;21(2): 156

COVID-19: Questionable Seasonality

Sadaf Sheikh

Department of Emergency Medicine, Sultan Qaboos University Hospital, Muscat, Oman

Dear Editor,

Variation in seasonality is one of key factor that play a role in viral transmission. Absence of herd immunity to Coronavirus disease-19 (COVID-19) suggest that it is weather resistant and spreading in population with no prior immunity (1). It is dangerous to rely on the assumption that it will end with the change of weather (1).

Our scientific understanding for COVID-19 transmission is fluid so it is advisable not to make assumptions about this virus and based our opinions with evidence. The appropriate way of reducing the transmission still based on personal protection (1,2).

A study showed an analysis from four different coronaviruses which were known to cause respiratory infections every year over a period of 8 years was performed (1). This analysis studied coronavirus occurrence and transmission in the cohort of households in Michigan (1-3). It showed that they are found in a limited time period. Time period mentioned in the study was through December to May reaching a peak from January to February. Analysis was designed to examine who influenza vaccine worked in their community. This analysis contained specimens which were followed on a weekly basis to get information about respiratory illnesses. Four highly seasonal coronavirus types were tested which were OC43, 229E, HKU1 and NL63 (1-4). 993 coronavirus infections were detected. OC43 was found to be most common type and 229E was the least common. There was a striking seasonal similarity between the four types with peak aggregate months between January and February (2-4). Children under 5 years got the highest frequency and 260 out of 993 patients acquired the infection from an infected household member. Infection rates level when age increases which were an unusual finding (2-4). They are very much related to SARS-CoV-19 virus and causing a milder illness (2,3). This led us to question how the current pandemic will evolve. If COVID-19 behaves like other seasonal coronaviruses, its cases may start to diminish by end of May or early June 2020, until transmission starts again in winter (4). Seasonality, even for common respiratory viruses, is a poorly understood phenomenon. While countries with temperate climate tend to have outbreaks of respiratory viruses during the colder season, transmission in tropical countries continues throughout the year. Also, sporadic outbreaks of respiratory viruses in the northern hemisphere in warmer weather have been reported related to cruise ships and air travel (2,3). A lot remains unknown. Which viral mutants survive and proliferate would certainly depend on that.

Sincerely,

Keywords: Seasonality, transmission, COVID-19

Ethics

Peer-review: Externally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

References

1. Sajadi M, Habibzadeh P, Vntzileos A, Shokouhi S, Miralles-Wilhelm F, Amoroso A. Temperature and latitude analysis to predict potential spread and seasonality for COVID-19. Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3550308. (Cited 2020 March 14).
2. Monto AS, DeJonge P, Callear AP. Coronavirus occurrence and transmission over 8 years in the HIVE cohort of households in Michigan. J Infect Dis. 2020:jiaa161. doi: 10.1093/infdis/jiaa161.
3. Guo YR, Cao QD, Hong ZS. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. Mil Med Res. 2020;7:11.
4. De Wit E, Van Doremalen N, Falzarano D. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;14:523-34.

Corresponding Author: Sadaf Sheikh, M.D., Department of Emergency Medicine, Sultan Qaboos University Hospital, Muscat, Oman
E-mail: sheikh.sadaf@gmail.com ORCID ID: orcid.org/0000-0001-7457-0012

Received: 07.02.2020
Accepted: 14.12.2020

Cite this article as: Sheikh S. COVID-19: Questionable Seasonality. Eurasian J Emerg Med. 2022;21(2):156.

EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2020.25349
Letter to the Editor
Eurasian J Emerg Med. 2022;21(2): 157

Point of Care Ultrasound in COVID-19 Pandemic

Sadaf Sheikh

Department of Emergency Medicine, Sultan Qaboos University Hospital, Muscat, Oman

Dear Editor,

Point of care ultrasound (POCUS) is useful to evaluate early lung changes in the emergency room in suspected Coronavirus disease-19 (COVID-19) patients. POCUS findings seem to be non-specific, microbiological confirmation is needed. Its unique feasibility where computed tomography (CT) chest is not available or in restricted use for infection control, makes it a non-invasive and cost-effective intervention. It can be used with a hope of reducing contamination of imaging room.

Using a 12-zone method, features are thickening of the pleural line with pleural line irregularity; B lines in a variety of patterns including focal, multifocal, and confluent; consolidations in a variety of patterns including multifocal small, non-translobar, and translobar with occasional mobile air bronchograms; appearance of A lines during recovery phase and pleural effusions are uncommon (1-3).

Nature of B lines if three or more per acoustic window, qualified for interstitial or alveolar-interstitial pattern. If homogenous interstitial pattern favors cardiogenic edema, heterogenous pattern with subpleural consolidation and pleural thickening is in favor of pneumonia or acute respiratory distress syndrome.

Literature of lung POCUS is showing promise. Huang et al. (2) showed that COVID-19 patients had infiltrations in bilateral lower lobes of lung. This study showed characteristic features such as bilateral B lines and subpleural consolidations consistent with CT chest. B lines are more fused and fixed as compared to pulmonary edema. Peng et al showed similar features in a multilobar pattern (2). Poggiali et al. (3) showed B lines and ground glass opacities.

Limitation of POCUS is that it is unable to detect deep lesions in the lungs. We believe that POCUS being ergonomically favorable with fewer infection control implications, there is a utility for rapid assessment of the patients in the emergency room, to review response during proning for better oxygenation and guide lung recruitment. It is also useful in evaluating undifferentiated shock, fluid tolerance, inserting and confirming central lines or intubations amidst global respiratory pandemic.

Keywords: POCUS, COVID-19, lungs

Ethics

Peer-review: Externally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

References

1. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. Intern Emerg Med. 2015;10:851-4.
2. Huang Y, Wang S, Liu Y, Zhang Y, Zheng C, Zheng Y, et al. A preliminary study on the ultrasonic manifestations of peri-pulmonary lesions of non-critical novel coronavirus pneumonia (COVID-19). Available from: https://ssrn.com/abstract=3544750 or http://dx.doi.org/10.2139/ssrn.3544750 [Preprint]
3. Poggiali E, Dacrema A, Bastoni D, Tinelli V, Demichele E, Ramos PM, et al. Can Lung US Help Critical Care Clinicians in the Early Diagnosis of Novel Coronavirus (COVID-19) Pneumonia?. Radiology. 2020;295:3. Doi: 10.1148/radiol.2020200847

Corresponding Author: Sadaf Sheikh, M.D., Department of Emergency Medicine, Sultan Qaboos University Hospital, Muscat, Oman
E-mail: sheikh.sadaf@gmail.com ORCID ID: orcid.org/0000-0001-7457-0012

Received: 23.07.2020
Accepted: 08.09.2020

Cite this article as: Sheikh S. Point of Care Ultrasound in COVID-19 Pandemic. Eurasian J Emerg Med. 2022;21(2):157.