ISSN 2149-2972
e-ISSN 2149-2980

koşuyolu heart journal

koşuyolu kalp dergisi

VOLUME 26
NUMBER 1
APRIL 2023
Published three time a year

www.kosuyoluheartjournal.com

koşuyolu heart journal

koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

VOLUME 26
ISSUE 1
APRIL 2023

Owner
Kartal Koşuyolu Yüksek İhtisas
Eğitim ve Araştırma Hastanesi

Editorial Office
Kartal Koşuyolu Yüksek İhtisas
Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli Kavşağı
Cevizli 34846 Kartal, İstanbul, Turkey
Phone : +90 216 500 1500 Ext: 5112
Fax : +90 216 500 1507
E-mail : info@kosuyoluheartjournal.com

bilimsel tıp yayınevi
www.bilimseltipyayinevi.com

Publisher
Bilimsel Tıp Yayınevi
Bükreş Sokak No: 3/20
Kavaklıdere-Ankara
Phone : +90 312 500 1500/1195
+90 312 466 23 11
Fax : +90 312 426 93 93
e-mail : bilimsel@bilimseltipyayinevi.com
Web : www.bilimseltipyayinevi.com

Publication Date ● April 2023

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

ABOUT JOURNAL

Koşuyolu Heart Journal is a peer-reviewed, open access e-journal that has been published three times a year in April, August and December. This is the scientific journal of the Health Sciences University Kartal Koşuyolu High Specialization Training and Research Hospital, (namely in Turkish, Sağlık Bilimleri Üniversitesi, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye).

The aim of the Koşuyolu Heart Journal; is to present advances in the field of cardiology, cardiovascular surgery, congenital cardiac surgery and cardiovascular anesthesia to the readers. Koşuyolu Heart Journal publishes research articles, reviews, original case reports and images, letters and critiques on cardiovascular medicine. The target reader population are the doctors specialized to the cardiovascular medicine. As an open access journal, all content is freely available.

Koşuyolu Heart Journal currently has an acceptance rate of 58%. The average time between submission and final decision is 40 days and the average time between acceptance and final printed publication is 13 weeks. However, provisional copy of submissions are published online within 1 month after acceptance.

Journal History :

- Koşuyolu Heart Journal, ISSN 1300-8706, 1990 - 2007.
- Koşuyolu Kalp Dergisi, ISSN 1300-8706, 2009 - 2014.
- Koşuyolu Heart Journal, ISSN 2149-2972, eISSN 2149-2980, 2015-2021.
- Koşuyolu Heart Journal, eISSN 2149-2980, since 2022

Indexing/Abstracting

TR Dizin, Index Copernicus, Dergipark, Türkiye Atıf Dizini and Turk Medline.

Submission Process: The manuscripts should be submitted via online.The journal do not charge any article submission or processing charges.

Subscription Procedures: All content of the Journal on this website is freely available without charge to the user or his/her institution.

Address: Koşuyolu Heart Journal, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Denizer Caddesi, Cevizli, 34846, Kartal, İstanbul/TURKEY

Phone: +90 216 500 1500 Ext: 5112

Fax: +90 216 500 1507

E-Mail: info@kosuyoluheartjournal.com

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

EDITORIAL POLICIES

Aims and Scope

Koşuyolu Heart Journal aims to present advances in the field of cardiology, cardiovascular surgery, congenital heart surgery, and cardiovascular anesthesia to the readers. In order to achieve this goal, Koşuyolu Heart Journal publishes research articles (for the clinical or laboratory studies), reviews (by invitation only), case reports, original images, original techniques for cardiovascular surgery or cardiovascular interventions and letters/critiques on cardiovascular medicine. Koşuyolu Heart Journal publishes, after double blinded peer review, the articles for the target reader population consisting of cardiologists, cardiovascular surgeons and cardiac anesthesiologists. The articles should be submitted in English, while the title and abstract should be written in both English and Turkish. Editorial and publication process of Koşuyolu Heart Journal are congruent with the standards of ICMJE, WAME, and COPE. Koşuyolu Heart Journal is an open access journal.

Originality of Manuscript

The corresponding author must certify that their article is original, has not been published previously, and is not under consideration for publication by another journal. The corresponding author should affirm originality of the work in the Article Submission Form. If the work has been presented previously at a meeting as an oral or poster presentation, corresponding author must state the name, date and place of the meeting at the Title Page.

Autorship

An individual who has made substantial intellectual contributions to the article should be an author. Each author must have a role in all of the following areas:

1. Conception and designing of study, or data collection, or analysis and interpretation of data.
2. Writing article or revising it substantially.
3. Final approval of the submitted version.

Other contributors who perform technical support, identify patients for study, translate the texts, supply materials, provide funding have not been qualified as author. These contributions may be acknowledged in the manuscript. Author roles are stated at Article Submission Form.

Human Rights

The Koşuyolu Heart Journal accepts the Declaration of Helsinki Principles as the policy of the Journal. Therefore, all studies concerning human subjects must be approved by the Institutional Review Board. All study subjects should be informed and written consent should be obtained. The editor may ask for a copy of the approval document.

Animal Rights

All studies dealing with animal subjects must be performed according to The Guide for the Care and Use of Laboratory Animals (https://www.nap.edu/catalog/5140/guide-for-the-care-and-use-of-laboratory-animals) with the approval of the Institutional Review Board. The editor may ask for a copy of the approval document.

Editorial and Peer Review Process

1. Tecnical review by the Editorial Secretary.
2. 1st review and similarity check by the deputy editor in chief (reject, sending technical revision or further evaluation)
3. Review by the Section Editor
4. Review by two external or more reviewers.
5. Review by Bioistatics Consultant (if required)
6. Revisions (if required)
7. Evaluation by the Section Editor (reject or accept)
8. Evaluation by the Editor-in-Chief (approval or reevaluation)
9. Assignment of DOI number
10. Appearance of article title and list of authors in Journal's website
11. English language editing
12. Galley proof preparation
13. Epub ahead of print
14. Publication

Authors and referees do not know each other's identities, journals follow a double-blind peer review process. All manuscripts submitted for publication are reviewed for their originality, methodology, ethical nature and suitability for the Koşuyolu Heart Journal. The editor has the right to format or reject the manuscripts which do not follow the rules or send them back to the author for correction. Authors who wish to withdraw their manuscripts need to state this to the editor in written form. All manuscripts received are submitted to iThenticate, a plagiarism checking system. Manuscripts judged to be plagiarised will not be considered for publication.

Submitted papers are reviewed by, the editor, the associated editors, and at least two reviewers. The editor and associated editors may decide to send the manuscript to a third reviewer. The editor and associated editors is the complete authority regarding reviewer selection. The reviewers may be selected from the Journals Advisory Boards or independent national or international reviewers may be selected when required for the topic of the manuscript. There are no submission and processing charges.

Instructions for Authors

Instructions for authors can be accessed from https://kosuyoluheartjournal.com/instructions-to-authors and printed samples of the Journal.

Scientific and Legal Responsibility of the Articles

Scientific and legal responsibility of the published articles belongs to the authors. Authors are responsible for the contents of the articles and accuracy of the references. Kartal Koşuyolu High Specialization Training and Research Hospital, the Editor-in-Chief, the Associated Editors or the Publisher do not accept any responsibility for the published articles.

Open Access Policy

Koşuyolu Heart Journal is an open access journal which means that all content is freely available without charge to the user or his/her institution. The Journal is licensed under CC BY-SA. The article content can be used provided that the Koşuyolu Heart Journal is cited. Journal articles can be archiving without any permission.

Citation

Koşuyolu Heart J

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

PUBLICATION ETHICS STATEMENT

The publication of an article in a peer-reviewed journal occurs with the scientific and ethical efforts of authors, reviewers, editors and publishers. Koşuyolu Heart Journal expects to carry out the stakeholders the following ethical responsibilities.

Authors' Responsibilities

1. The work submitted for publication must have not been published in another journal or submitted at the same time. Each application can be started following the completion of the previous application. Published work in another journal can not be sent to Koşuyolu Heart Journal.
2. Author(s) are required to make use of and / or quote in a complete and accurate way in order to benefit from other studies or to use other studies.
3. If all work submitted for publication is to constitute a conflict of interest, and if relevant, should be indicated.
4. The author(s) may request raw data on their framing of evaluation processes; in such a case the author(s) should be ready to submit the expected data and information to the editorial board.
5. The author(s) must have evidence that they have the necessary permissions for the use rights of the data used, research / measurement tools / analyzes.
6. The author(s) has an obligation to cooperate with the editor in informing, correcting or withdrawing the journal editor or publisher if he / she finds a mistake or error related to his / her early published or evaluation work.

Reviewers' Responsibilities

1. Admit only to evaluate the work related to the field of expertise.
2. It should evaluate within impartiality and confidentiality.
3. If he / she thinks that he / she is confronted with a conflict of interest during the evaluation process, he / she should refuse to examine the work and inform the editor of the journal.
4. The privacy policy should destroy the work that has been reviewed by the review process. Only the final versions of the studies can be used after publication.
5. Assessment should be done objectively only with respect to the content of the work. Nationality, gender, religious beliefs, political beliefs and commercial concerns should not allow it to influence the evaluation.
6. Use a polite language when making an assessment. Avoid humiliating personal interpretations of hostility, slander and insults.
7. The evaluation should be carried out on time and on the above ethical responsibility.

Editors' Responsibilities

1. All publications are judged on the basis of their intellectual content, regardless of the author's gender, race, ethnicity, religion, citizenship and political values.
2. Personal information about the articles is kept confidential.
3. The conflict of interest observed regarding the article must be explained.
4. The Editorial Board assumes the responsibility to make publishing decisions for the submitted articles, based on the evaluation of the candidate's articles, the editorial board policies of the journal, and the legally prohibited items against plagiarism and copyright infringement.

Publishers' Responsibilities

1. The publisher has a supporting role in the scholarly communication process between editors, referees and authors.
2. The publisher provides the editors with similarity check reports for all submissions to our editorial systems.
3. The publisher should not interfere with the editorial decision.

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

INSTRUCTIONS for AUTHORS

Scope of the Journal

The Koşuyolu Heart Journal is published three times a year (april, august, and december). The journal accepts articles in English language. However, the articles have the titles and abstracts written in English and Turkish language. Terms written in another language should be indicated within quotation marks in articles.

All manuscripts submitted for publication should comply with Uniform Requirements for Manuscripts Submitted to Biomedical Journals produced and updated by the International Committee of Medical Journals Editors (http://www.icmje.org/).

The Koşuyolu Heart Journal accepts the Declaration of Helsinki Principles (http:// www.wma.net/en/30publications/10policies/b3/index.html) as the policy of the Journal. Therefore, all manuscripts concerning human subjects must contain a statement in the Materials and Methods section, indicating that the study was approved by the Institutional Review Board. All study subjects should be informed and written consent should be obtained and this should be declared in the Materials and Methods section. All manuscripts dealing with animal subjects must contain a statement indicating that the study was performed according to The Guide for the Care and Use of Laboratory Animals (https://www.nap.edu/catalog/5140/guide-for-the-care-and-use-of-laboratory-animals) with the approval of the Institutional Review Board, in the Materials and Methods section. The Editor may ask for a copy of the approval document. The journals editorial and publication process are also congruent with COPE (https://publicationethics.org/guidance/Guidelines) standards.

Submission Process

The manuscripts should be submitted via online manuscript evaluation system (https://submit.kosuyoluheartjournal.com).

Forms

An "Article Submission Form" consisting of author role, originality, and conflict of interest disclosure, signed by the corresponding author, declaring that the manuscript has not been published or is not currently submitted to another journal and that the manuscript is approved by all the authors. The Article Submission Form should be simultaneously uploaded together with manuscript files.

Koşuyolu Heart Journal "Copyright Transfer Form" might be uploaded together with manuscript files or should be sent after acceptance of the manuscript via e-mail to info@kosuyoluheartjournal.com. After submission of the copyright transfer form signed by each author, changes of authorship or in the order of the authors listed will not be accepted by Koşuyolu Heart Journal.

These forms are available on https://submit.kosuyoluheartjournal.com.

Manuscript Preparation

Style and Format: The manuscript text should be written in Times New Roman font, 12 point-type, double-spaced with 2 cm margins on the left and right sides. The article should be prepared with Microsoft Words. The pages should be numbered starting with the title page. Page numbers should appear at the bottom right corner of every page. The main text file should not contain any information regarding author names and affiliations.

Symbols, Units, and Abbreviations: In general, the Journal follows the conventions of Scientific Style and Format, The CSE Manual for Authors, Editors, and Publishers, Council of Science Editors, Reston, VA, USA (7th ed.). Please use SI units. Abbreviations should be internationally accepted and should be defined accordingly in the text in parenthesis when first mentioned and used in the text. The abbreviated form should be used all throughout the article.

Title Page: Title page of the manuscript should include the Turkish and English title of the article, Turkish and English running title not exceeding 40 characters including spaces as well as the full names, surnames and academic degrees of the authors. The department, division and institution of the authors should be indicated. Title page should also include address, e-mail, phone and fax number of the corresponding author. Authors should indicate the name, the date, and the place of the meeting if the research has been presented previously in a congress or symposia. Title page should be submitted as a separated file.

Abstracts: All manuscripts should be in Turkish and English abstracts. Abbreviations should be avoided as much as possible. References, figures, tables and citations should not be used.

Keywords: There should be two to five key words complying with the Index Medicus Medical Subject Headings (MeSH) and Türkiye Bilim Terimleri for Turkish. Refer to https://meshb.nlm.nih.gov/search and https://www.bilimterimleri.com for English and Turkish key words, respectively.

Original Investigations are clinical or experimental research articles. They should include; Turkish title, Turkish structured abstract (limited to 300 words structured as Giriş, Hastalar ve Yöntem, Bulgular and Sonuç), Turkish key words and English title, English structured abstract (limited to 300 words structured as Introduction, Materials (or Patients) and Methods, Results and Conclusion), English key words. The other sections of the manuscript should include Introduction, Materials (or Patients) and Methods, Results, Discussion, Acknowledgement (if required) and References. All sections of the manuscripts should start on a new page. Research articles are not referred to exceed 5000 words and 40 references.

Reviews: Manuscripts in the form of Reviews are accepted when invited since 2009. In case of wishing to write a review about a current topic without being invited, the editor and the associate editors should be contacted before the manuscript is submitted. Review Articles should include; Turkish title, Turkish abstract, Turkish key words and English title, English abstract and English key words. The abstract should be prepared as one paragraph in Review type articles and limited to 300 words. Structured abstract is not required. Number of references should be limited to 40 if possible.

Case Reports should include Turkish title, Turkish abstract, Turkish key words, English title, English abstract, English key words, Introduction, Case presentation, Discussion and References. Introduction and Discussion sections of the Case reports should be short and concise and the abstract should be prepared as one paragraph. Structured abstract is not required. Case reports should not exceed 1500 words and the number of references should not exceed 20.

Original Techniques should include Turkish title, Turkish abstract, Turkish key words, English title, English abstract, English key words, Introduction, Technique, Discussion and References. Introduction and Discussion sections of the Original Techniques should be short and concise and the abstract should be prepared as one paragraph. Structured abstract is not required. Original Surgical Techniques should not exceed 1500 words and the number of references should not exceed 10.

Original Images in cardiovascular system are images dealing with related subjects. The title should not contain more than eight words. No more than three authors may be listed. The legend should not exceed 150 words. The legend to the image should succinctly present relevant clinical information, including a short description of the patients history, relevant physical and laboratory findings, clinical course, response to treatment (if any), and condition at last follow-up. All labeled structures in the image should be described and explained in the legend. The number of references should not exceed 3 and not include an abstract. Running title is not required.

Letter to the Editor: Readers are encouraged to write about any topic that relates to cardiology, cardiovascular surgery, and cardiovascular anesthesiology and may include discussions on material previously printed in the Journal. Letter to the Editor should be short and concise limited to 1000 words and 5 references. Abstract is not required.

Tables and Figures: Tables, figures, graphics and pictures should be numbered with Arabic numbers in order of reference in the text. Localization of tables, figures, graphics and pictures should be indicated.

Each table should be prepared with double spacing on a separate page. Tables should have a brief title. Authors should place explanatory matter in footnotes not in the heading. Explanations should be made for all nonstandard abbreviations in footnotes. The following symbols should be used for abbreviations in sequence: *,

#. Each table should be cited in text.

Figures should be either professionally drawn or photographed, and these items should be submitted as photographic-quality digital images. Figures should be submitted in a format that will produce high-quality image (for example, JPEG or GIF). Authors should control the images of such files on a computer screen before submitting them to be sure they meet their own quality standards. Information on staining and microscopic images, the magnification ratio.

X-ray films, scans and other diagnostic images, as well as pictures of pathology specimens should be submitted as sharp, glossy, black-and-white or color photographic images. Letters, numbers, and symbols on figures should be clear and consistent

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

throughout, and large enough to remain legible when the figure is reduced for publication. Figures should be made as self-explanatory as possible. For recognizable photographs of patients, signed releases of the patient or of his/her legal representative should be submitted; otherwise, patient names or eyes must be blocked out to prevent identification.

Legends for figures, graphics and pictures should be typed starting on a separate page, double spaced, indicating the corresponding illustrations with numbers. When symbols, arrows, numbers or letters are used to identify parts of illustrations, define each one clearly under the illustration. If quoted parts, tables, figures, graphics, pictures etc exist in the manuscript, the authors should obtain written permission from the author and copyright holder and indicate this.

Acknowledgements: All the entities that provide contribution to the technical content, data collection and analysis, writing, revision etc. of the manuscript and yet do not meet the criteria to be an author should be mentioned in the acknowledgement part. If the contribution of the sponsor is only in the form of financial support, this should be stated in the Acknowledgement section. If the sponsor has participated in the methods, statistical analysis or manuscript preparation, this contribution should also be stated in the Materials and Methods section. If there is no conflict of interest it should also be stated.

References: Data and manuscript not published yet should not be included among the references. These should be stated in the main text as "author(s), unpublished data, year".

Reference numbers should be indicated at the end of the sentences in the text as superscripts and references should be numbered consecutively in the order they are mentioned in the text. Journal names should be abbreviated as listed in "Index Medicus" or in "ULAKBIM/Turkish Medical Index". References should be typed in consistence with the following examples. Native references should be used as much as possible.

If the reference is a journal;

Author(s)' surname and initial(s) of the first name (all authors if the number of authors are 6 or less, first 6 authors if the number of authors of an article is more than 6 followed by "et al."). Title of the article, title of the manuscript abbreviated according to Index Medicus (http://www.ncbi.nlm.nih.gov/sites/entrez/query.fcgi?db=nlmcatalog). Year;Volume:First and last page number.

Example: Suárez De Lezo J, Medina A, Pan M, Romero M, Segura J, Pavlovic D, et al. Transcatheter occlusion of complex atrial septal defects. Catheter Cardiovasc Interv 2000;51:33-41.

If the reference is a journal supplement;

Author(s)' surname and initial(s) of the first name. Title of the article. Title of the manuscript abbreviated according to Index Medicus (http://www.ncbi.nlm.nih. gov/sites/entrez/query.fcgi?db=nlmcatalog). Year;Volume(Suppl Supplement number):First and last page number.

Example: Parsonnet V, Lean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation 1989;79(Suppl 1):S3-S12.

If the reference is a book;

Author(s)' surname and initial(s) of the first name. Title of the book. Edition number. City of publication, Country: Publisher, Year of Publication: Page numbers.

Example: Borrow K, Braunwald E. Heart Disease. 1st ed. Philadelphia, PA, USA: WB Saunders, 1988:976.

If the reference is a book chapter;

Surname and initial(s) of the first name of the author(s) of the chapter.Title of the chapter. In: Surname and initial(s) of the first name(s) of the editor(s) (ed) or (eds). Title of the book. Edition number. City of publication, Country: Publisher,

Year of publication: First and last page numbers of the chapter.

Example: Nguyen A, Imoto E, Eklof BGH. Pulmonary embolism. In: Barros DSa AAB, Chant ADB (eds). Emergency Vascular and Endovascular Surgical Practice. 2nd ed. London, UK: Hodder Arnold, 2005:251-60.

If the reference is an article presented in a meeting;

Author(s)' surname and initial(s) of the first name (all authors if the number of authors are 6 or less, first 6 authors if the number of authors of an article is more than 6 followed by "et al." in international references).Title of the article, If applicable In:Surname and initial(s) of the first name(s) of the editor(s) (ed) or (eds). Title of the book. Title of the meeting; Date; City of the meeting; Country.

Publisher; Year. Page numbers.

Example: Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Reinhoff O (eds). MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10; Geneva, Switzerland. North-Holland; 1992. p. 1561-5.

If the reference is an online journal;

Author(s)' surname and initial(s) of the first name (all authors if the number of authors are 6 or less, first 6 authors if the number of authors of an article is more than 6 followed by "et al." in international references). Title of the article, title of the manuscript abbreviated according to Index Medicus Year; Volume (Number). Available from: URL address. Accessed date:day. month.year.

Example: Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis 1995;1(1). Available from: http://www/cdc/gov/ncidoc/EID/eid.htm. Accessed date: 25.12.1999.

If the reference is a website;

Name of the web site. Access date. Available from: address of the web site.

Example: World Health Organization (WHO). Access date: 9 July 2008. Available from: http://www.who.int

If the reference is a thesis;

Author's surname and initial of the first name. Title of the thesis (Thesis). Name of the university (or educational hospital, institution, etc), City, Country, Year.

Example: Kalender M. The effect of using internal mammarian artery graft on coronary bypass morbidity and mortality in octogenarian. (Thesis). Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye, 2011.

Reprints

Reprint of the article is not sent to the authors. The issue of the journal is sent by Publishing House.

Correspondence Address

Manuscript can only be submitted through our online system. Other correspondence may be directed to: e-mail: info@kosuyoluheartjournal.com or Koşuyolu Heart Journal, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Denizer Caddesi Cevizli Kavşağı No: 2, Cevizli 34846 Kartal, İstanbul, Türkiye.

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

COPYRIGHT TRANSFER FORM

Manuscript Title: .....
.....
Manuscript Number: .....

By submitting this form, each author agrees with the copyright to this article transferred to Kosuyolu Heart Journal, the scientific publication of Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi.

The authors warrants that their contributions are original. Each author signs for and accepts responsibility for releasing this material. The copyright transfer covers the right and license to reproduce, publish, distribute and archive the article in all forms and media expression.

After submission of the agreement signed by each author, changes of authorship or in the order of the authors listed will not be accepted by Koşuyolu Heart Journal.

Authors :

Each author must sign in according to the order of authors list.

Name, Surname	ORCID ID	Sign
1.	.....	.....
2.	.....	.....
3.	.....	.....
4.	.....	.....
5.	.....	.....
6.	.....	.....
7.	.....	.....
8.	.....	.....
9.	.....	.....
10.	.....	.....

Copyright Transfer Form signed by all authors must be returned to the Koşuyolu Heart Journal via manuscript submitting system.
e-mail: info@kosuyoluheartjournal.com
Fax: +90 216 500 1507

www.kosuyoluheartjournal.com

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

ARTICLE SUBMISSION FORM

Manuscript Title .....

.....

By submitting this form, the corresponding author acknowledges that each author has read and agrees with the information contained in the Originality, Author Role and Competition of Interest Form completed at the time of initial manuscript submission.

Originality of Research

The authors certify that this manuscript is original, has been written by the stated authors, has not been published previously, and is not under consideration for publication by another journal. If parts of the work or patients included in this manuscript have been previously published, the authors are required to disclose this information to the Editors.

Authorship

Koşuyolu Heart Journal has required that authors specify their roles and meet the requirements for authorship as listed in the "Uniform Requirements for a Manuscript Submitted to Biomedical Journals." These indicate that each author must contribute to a manuscript in each of the following 3 areas:

1. Substantial contribution to conception and design; or acquisition of data; or analysis and interpretation of data.

2. Drafting the article or revising it critically for important intellectual content.

3. Final approval of the version to be published.

If someone has contributed to the manuscript but does not meet these criteria, they should be listed in the Acknowledgements section rather than on the author byline.

Author Role

Koşuyolu Heart Journal requires that the corresponding author complete the statement below, filling in the blanks with the appropriate author initials This statement will be reproduced at the end of your manuscript in the printed and online journal, just prior to the reference section, for all clinical and basic research manuscripts. The overall responsibility line should list the single individual who guarantees the scientific integrity of the work as a whole. All other blanks should be completed as necessary, by all authors who played a significant role in that capacity. Please list only 2 initials for each author, without periods, but separated by commas (e.g. MY, HS). In the case of two authors with the same initials, please use their middle initial (e.g. AME, ASE), or full names to differentiate between them.

Conception and design: ___
Analysis and interpretation: ___
Data collection: ___
Writing the article: ___
Critical revision of the article: ___
Final approval of the article: ___
Statistical analysis: ___
Obtained funding: ___
Overall responsibility: ___

Competition of Interest Disclosure

The Journal requires that each author disclose any sponsor that provided financial support for the study. Such a statement should indicate the details of corporate funding, as well as any involvement by a sponsor of this study in the design; collection, analysis, and interpretation of data; manuscript writing; or the decision to submit the manuscript for publication. This information must be included below in the Competition of Interest statement.

In addition, the Journal requires that each author disclose any personal financial arrangements that might be perceived as a competitive interest with respect to this study. Specifically, for each author:

1. Has the author received a financial contribution from a company or organization that might benefit (or lose) financially from the results, conclusions or discussion presented in the paper/letter? Examples include:
   - royalties
   - patents (or patents pending)
   - fees for consulting
   - fees for speaking when organized by a corporate sponsored speakers' bureau
   - funds for a member of the author's staff or family

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

2. Does the author own stocks, shares or have options in a company or organization that might benefit (or lose) financially from the results, conclusion or discussion presented in the paper/letter?

3. Does the author have any other competing financial interests that should be disclosed? In response to these questions, you must check one of the boxes below:

…… No The authors have no competing interests to declare. Please print "No competing interest declared" with the article

…… Yes The authors do have competing interests to declare. Please print the following statement with the article:

Example: "CK has been paid a consulting fee by ABC Company and is on their speakers bureau; ASE has shares in the company; AH received funding for a research assistant from the ABC Company. The study was funded by corporation ABC."

Although the above language emphasizes financial disclosure, each author may choose to disclose other potential conflicts which could include an academic association or antagonism with someone whose interest might be affected by the publication, membership in a special interest group whose interests might be affected by the paper, or other strong convictions that might have affected.

Ethical Approval

All of the original investigations concerning human subjects and the laboratory animals must be approved by the Institutional Review Boards.

The name of Review Board:

Approval document number and date:

Corresponding author signature: **Date: (Day/Month/Year)**

Contact Address
Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Denizer Caddesi Cevizli 34846 Kartal, İstanbul, Turkey
Phone: +90 216 500 1500 Ext: 5112 **Fax:** +90 216 500 1507 **E-mail:** info@kosuyoluheartjournal.com

koşuyolu heart journal
koşuyolu kalp dergisi

ISSN 2149-2972
e-ISSN 2149-2980

CONTENTS / İÇİNDEKİLER

VOLUME 26
NUMBER 1
APRIL 2023

Survey-Based Evaluation of Cancer Patients' Satisfaction and Discomfort Experienced During Central Venous Port Use

İbrahim Çağrı Kaya(İD)

Eskişehir City Health Application and Research Center, Eskişehir, Türkiye

ABSTRACT

Introduction: The use of central venous port provides a safer and better quality of life for cancer patients undergoing chemotherapy. Refusal of central venous port implantation in patients with inadequate venous access may lead to discontinuation of chemotherapy or even extravasation of peripheral vasculitis and anti-cancer drugs. By doing this survey-based study, it was aimed to determine the reasons before the implantation of central venous port systems, the patient's satisfaction afterwards, the complications associated with the port system, the discomfort they cause and the expectations of the patients.

Patients and Methods: The study was carried out based on a questionnaire and through one-to-one interview by a cardiovascular surgeon with 100 patients who were treated with central venous port in the chemotherapy unit of Eskişehir City Hospital between August 1 and October 31, 2022.

Results: Sixty-one percent of the patients cited long-term intravenous therapy and 44% cited inadequate venous access as the cause of port implantation. Ninety-six percent of the participants stated that they were satisfied with their ports. Only six patients stated that they had various problems, but were satisfied overall. When asked about the advantages of using the port, 76% of the patients stated that they no longer had more than one vascular puncture problem and 75% stated that they felt less pain. Fifty-one percent of the patients stated that they felt anxiety before the procedure; the most felt concern was possible complications (13 patients) and the thought that it would cause discomfort in life. Nine patients experienced complications after port implantation. Five patients described port system obstruction and four patients described the development of skin infection.

Conclusion: Especially in our country, most patients still do not use central venous ports. The fact that existing fears and anxiety of the patients before the procedure cannot be eliminated with adequate and correct information plays an important role in this. At this point, the operator who performs the surgical procedure in the center where the procedure is performed should inform the patient and the oncology and chemotherapy nurse who give first information to the patient.

Key Words: Chemotherapy, central venous catheter, port catheter

Kanser Hastalarının Santral Venöz Port Kullanımı Sırasında Yaşadıkları Memnuniyet ve Rahatsızlığın Ankete Dayalı Değerlendirmesi

ÖZET

Giriş: Santral venöz port kullanımı, kemoterapi gören kanser hastalarında daha güvenli ve kaliteli bir yaşam olanağı sunmaktadır. Yetersiz venöz erişim sorunu olan hastalarda santral venöz port implantasyonunun reddedilmesi, kemoterapinin kesilmesine hatta periferik vaskülit ve anti-kanser ilaçların ekstravazasyonuna yol açabilir. Ankete dayalı bu çalışmayı yaparak; santral venöz port sistemlerinin implantasyonundan önce nedenleri, sonrasında hastanın memnuniyeti, port sistemi ile ilişkili komplikasyonlar, neden oldukları rahatsızlık ve hastaların beklentilerini tespit etmeyi amaçladık.

Hastalar ve Yöntem: 1 Ağustos ve 31 Ekim 2022 tarihleri arasında Eskişehir Şehir Hastanesi Kemoterapi Ünitesinde tedavisini santral venöz port ile alan 100 hasta ile bir kalp ve damar cerrahisi uzmanı tarafından bire bir görüşme yoluyla, ankete dayalı olarak gerçekleştirildi.

Bulgular: Hastaların %61'i port implantasyon sebebi olarak uzun süreli intravenöz tedaviyi, 44'ü yetersiz venöz erişimi gösterdi. Ankete katılanların %96'sı portundan memnun olduğunu söyledi. Yalnız altı hasta çeşitli problemler yaşadığını fakat yine de memnun olduğunu belirtti. Port kullanımının avantajları sorulduğunda hastaların %76'sı artık birden fazla damar delinme sorunu yaşamadığını, %75'i daha az ağrı hissettiğini belirtti. Hastaların %51'i işlem öncesi endişe hissettiğini belirtti; en çok hissedilen endişe gelişebilecek komplikasyonlar (13 hasta) ve günlük hayatta rahatsızlık vereceği düşüncesiydi. Port implantasyonu sonrası dokuz hasta komplikasyon yaşamıştı. Beş hasta port sistemi tıkanıklığı, dört hasta da ciltte enfeksiyon gelişimi tarifledi.

Sonuç: Özellikle ülkemizde halen hastaların büyük bir bölümü santral venöz port kullanmamaktadır. Bunda hastaların işlem öncesi mevcut korku ve anksiyetelerinin, yeterli ve doğru bilgilendirme ile giderilememesi önemli bir rol oynamaktadır. Bu noktada özellikle işlemin yapıldığı merkezde cerrahi prosedürü uygulayan operatörün hastayı ve hastaya ilk bilgiyi veren onkoloji ve kemoterapi hemşiresini çok iyi bilgilendirmesi gerekmektedir.

Anahtar Kelimeler: Kemoterapi, santral venöz kateter, port kateter

Cite this article as: Kaya İÇ. Survey-based evaluation of cancer patients' satisfaction and discomfort experienced during central venous port use. Koşuyolu Heart J 2023;26(1):1-6.

Correspondence

İbrahim Çağrı Kaya

E-mail: icagrikaya@gmail.com
Submitted: 19.11.2022
Accepted: 22.11.2022
Available Online Date: 21.03.2023

INTRODUCTION

In recent years, the use of central venous port (CV port) systems has increased rapidly due to their convenience and safety in patients requiring long-term continuous intravenous therapy and in patients with difficult venous access[1]. The use of CV port offers a safer and better quality of life for patients with cancer undergoing chemotherapy. Providing continuous, reliable intravenous catheterization has given clinicians the opportunity to apply more complex and more effective treatment regimens. On the other hand, it has created the opportunity for outpatient treatment and shortened hospital stay[2]. An advanced medical center in Japan states that patients refuse to have CV ports implanted for various reasons, such as fear of complications or avoidance of implanted artificial devices[3]. Refusal of CV port implantation in patients with inadequate venous access may lead to discontinuation of chemotherapy or even peripheral vasculitis and extravasation of anti-cancer drugs.

We found that some of the patients who were requested to have CV port implantation for various clinical reasons in our hospital hesitated to approve the procedure, some did not accept due to their fears, but after port implantation, these patients gave feedback with great satisfaction and saw that the CV port could be used for many different purposes. Therefore, by doing this survey-based study, we aimed to determine the reasons before the implantation of CV port systems, the patient's satisfaction afterwards, the complications associated with the port system, the discomfort they caused, and the expectations of the patients.

PATIENTS and METHODS

Subjects and procedures

This study was carried out between August 1, 2022 and 31 October 1, 2022 in Eskişehir City Hospital Cardiovascular Surgery Outpatient Clinic and Chemotherapy Unit. All patients who received chemotherapy with the CV port system during this period were included in the study. The questionnaire was personally conducted by a cardiothoracic surgeon in the cardiovascular surgery outpatient clinic and chemotherapy unit. Written consent form was obtained from all participants before starting the survey.

Surgical Procedure

All patients with CV port implanted by us were operated with the same surgical technique by a single operator. Surgical procedure was performed under local anesthesia with Doppler ultrasonography and scopy support in the angiography unit or operating room conditions. The jugular vein was preferred as venous access. The patient was followed up in service conditions for at least four hours after the procedure and was discharged after having seen control chest X-ray and heart teleradiogram. Routine antibiotic prophylaxis before the operation and maintenance antibiotic therapy were not applied afterwards.

Questionnaire

The questionnaire was developed by the researchers by utilizing similar studies and arranged according to the socioeconomic and literacy level of the patient group (Table 1)[4]. Sex, age group, number of port implantation procedures the patient underwent, the environment where the port was implanted (inpatient or outpatient), reasons for port implantation, patient's satisfaction with the CV port, discomfort, patient's opinion of the advantages of the CV port, any concerns the patient had prior to port implantation, and the patient's expectations about the CV port were questioned.

Statistical Analysis

All statistical analyzes were performed using "IBM SPSS Statistics version 23". Descriptive statistics were used to characterize the patient population. In all analyses, $p< 0.05$ was considered significant.

RESULTS

As planned before, 100 patients who had been admitted to the chemotherapy unit and cardiovascular surgery outpatient clinic of our hospital and had agreed to participate in the survey were included in the study. Table 2 shows patient characteristics. Sixty-five of the patients were males and 35 were females. Vast majority of the patients were in the 40/59 age group (44 patients). When asked about the reason for CV port implantation, 61 of the patients stated their reason for preference as long-term intravenous therapy and 44 patients as poor venous access (they were allowed to choose more than one reason) (Table 2). Four of our patients stated that they had a second port implantation procedure. While an interventional radiologist performed the CV port implantation operation in five of the patients, this procedure was performed by a cardiovascular surgeon in 95 patients. While 90 patients' surgeries were performed in our hospital, 10 patients stated that their CV port was implanted in another center. In addition, 54 and 46 patients had CV ports implanted as inpatients and outpatients, respectively.

Of the patients, 96% stated that they were satisfied with their port, while six patients stated that they were partially satisfied but had some problems. No patient regretted port implantation. The patient, who was less satisfied than the others, stated that he had problems because an infection had developed at the surgical incision site. Patients were asked to indicate their satisfaction level on a scale of 0-100%. The sat-

Table 1. Questionnaire applied to the patients in the study.

Please answer the following questions to assist our clinical investigation of the use of central venous ports for chemotherapy.

1. How long ago your central venous port was inserted?
   1) <1 month 2) 1-3 months 3) 3-6 months 4) >6 months

2. Was your santal venous port inserted in our hospital?
   1) Yes 2) No

3. Who inserted your port?
   1) Cardiovascular surgeon 2) Radiologist 3) Other

4. a. What is your gender? b. What age group do you belong to? c. How many times have ports been implanted in your body?
   a. 1) Male, 2) Female
   b. 1) <20 years, 2) 20-39, 3) 40-59, 4) 60-79, 5) >80
   c. 1) Once, 2) Two times, 3) Three or more times

5. When your port was implanted, were you an inpatient or an outpatient?
   1) Inpatient, 2) Outpatient

6. Why was your port implanted?
   A) It made it difficult for me to get intravenous infusions as my veins were thin and weak.
   B) Because I needed long-term continuous intravenous therapy.
   C) Other reasons

7. How satisfied are you with the port system in general?
   1) I am very happy with the port system and wish it was implamented earlier
   2) I am satisfied with the CV port system.
   3) I am somewhat satisfied with the CV port system, but have had some discomfort.
   4) I regret that the CV port system was implanted.

8. If you chose option 3) or 4) for Question 7, please describe the discomfort you are experiencing.
   (...)

9. If full satisfaction is defined as 100% and complete dissatisfaction as 0%, how satisfied are you with the port system?
   (...%)

10. Please choose the advantages of the ports that suit you (you can choose more than one answer).
    1) I no longer have to go through multiple venipuncture procedures.
    2) I feel less pain when the procedures are done through my port rather than my peripheral veins.
    3) I do not have to adjust the position of my arms during intravenous injections.
    4) The port does not bother me much in my daily life.
    5) Other reasons (...)

11. Did you have any concerns before the port system was implanted?
    1) I didn't feel any anxiety.
    2) I felt some anxiety.

12. If you chose option 2) for Question 11, what is the source of your concern? (you can choose more than one answer)

    1) There was no obvious reason, but I felt a vague sense of anxiety.
    2) I received insufficient information about the port system from the health personnel.
    3) I was afraid of complications.
       (Please explain what kind of complications you are afraid of: ...)
    4) Admission to the hospital for port implantation was not suitable for me.
    5) I was afraid of cosmetic deformities.
    6) I was afraid that the port might disturb me in my daily life.
    7) I would not trust medical personnel.
    8) The idea of having an artificial device in my body bothered me.
    9) Other types of anxiety (...)

13. Have you had any complications with the port system?
    1) Port system obstruction, 2) Infection, 3) Twisting or opening of the skin 4) Other complications (...)

isfaction levels of patients who underwent port implantation due to poor venous access, need for long-term intravenous treatment and other reasons were 96.7%, 95.4% and 95%, respectively, and there was no significant difference in terms of the satisfaction levels between patient groups (Table 3).

When answers regarding the advantages of CV port usage were evaluated, 76 of the patients stated that they no longer had multiple venipuncture procedures and 75 stated that they felt less pain (Table 4).

Table 2. Patients' characteristics

		n (%)
Sex	**Female/Male**	**35/65**
Age	20-39/40-59/60-79	13/44/43
Reason of implantation	Poor venous access/longterm IV therapy	44/61
Implantation setting	Inpatient/outpatient	54/46

Table 3. Satisfaction score

Reason	Number	Mean %	SD	p
Poor venous access	44	96.7	2.6	0.41
Longterm cont. IV therapy*	61	95.4	4.1	

*longterm continuous intravenous therapy,
p values were calculated using Student's t-test.

Table 4. Advantages of using a central venous port

1.	Multiple venipuncture procedures are no longer required	76
2.	Patients describe less pain sensation.	75
3.	Patients do not have to adjust the positions of their arms during intravenous injections	57
4.	In my daily life, the CV port does not cause much discomfort.	64

When the patients were asked if they had any concerns before the procedure, 51 stated that they felt anxiety (Table 5). The most felt concerns were complications that might develop during the procedure (13 patients) and that the port would cause discomfort in their daily lives (13 patients).

Nine patients answered "yes" to the question "Did you experience any complications after CV port implantation?". Four of these patients stated that the port system was blocked, and five of them stated that they developed a skin infection. In four of the patients, infection developed in the occlusion and incision line in the CV port systems, and infection developed in the incision line only in three patients. In two of our patients, due to the leakage of the chemotherapy drug under the skin, infection and opening at the incision site developed, and wound revision was required.

DISCUSSION

Recently, the use of CV ports has increased, especially in Western countries. However, this rate is not yet at the desired level in our country. In a New York-based study conducted by Snyderman et al. on 18.000 patients, the rate of CV port usage varies between 24-56% according to cancer types[5], and this rate has been found to be 15% in an India-based study by Madabhabi et al[6]. Robinson's meta-analysis published in 2018 showed that patients with cancer preferred more CV ports as socio-economic level and literacy rate increased[7]. In our

Table 5. The source of anxiety felt before the procedure

Source	n
Vague anxiety with no clear cause	35
Insufficient information about the CV port	10
Possibility of complications	13
Cosmetic deformities	5
Disturbances to daily life	13
Aversion to the implantation of artificial devices	5

Table 6. Comparison of "PORT" study results with international studies

Character	Madabhavi et al. (%)	Vardy et al. (%)	Present study (%)
No. of cases	100	110	91
Antibiotic prophylaxis	100	NA	NA
Infection	8	4	9.8
Catheter fracture	2	2	NA
Catheter displacement	2	NA	NA
Thrombosis	1	2	4.3

center, 208 (17.3%) of 1200 patients who received chemotherapy between February 1 and June 1 received their treatment with a CV port. In the study conducted by Yesilbalkan et al. on patients in our country, it has been shown that patients do not prefer CV port because they do not have sufficient information before the procedure[8].

In our study, before port implantation, vague anxiety with no clear cause (35%) was the most common type of anxiety, which was followed by the possibility of complications (13%) and the fear of discomfort in daily life (13%). After port implantation, 96% of patients stated that they were satisfied with their port. This rate was higher than similar studies conducted in Europe[9,10].

Considering the satisfaction rates according to port implantation preference reasons, the highest satisfaction rate was in the patient group with poor venous access. However, there was no statistically significant difference between the groups. Based on this, we can say that port implantation should be preferred in the early period in elderly patients, obese patients and patients with peripheral vascular access problems.

CV port implantation was performed in 91 of the patients included in the study by a cardiovascular surgeon in our hospital, and the procedure was performed in nine patients by an interventional radiology specialist in another center. Ninety-one patients who underwent port implantation procedure in our hospital were compared with two international studies according to the character of the complications (Table 6)[6,11]. While catheter malposition and breakage were never seen in our patient group, our rates of catheter thrombosis and incision site infection were higher than in those studies. Due to our results, it was decided to provide training on port catheter care and cleaning the port correctly in the same way by all nurses after the treatment session. Since our preference for antibiotic prophylaxis was thought to be a factor in our higher infection rate, it was decided to start routine prophylaxis in each patient after our study.

In the interviews we made for this study, we found that the patients who decided to have CV port implantation were evaluated and informed by the oncology clinic and our physicians and that the patients were most worried and afraid about the surgical procedure. In the light of these data, we made some more satisfactory arrangements about giving preoperative information with our physicians in the oncology unit and nurses in the chemotherapy unit.

When we evaluated the opinions of the patients regarding the advantages of their ports, the most commonly reported advantages were that they did not need more than one venipuncture, they felt less pain, and they did not feel discomfort in their daily lives, respectively. In a similar study by Yagi et al., the most common advantage reported was not having to adjust the positions of the arms during intravenous injection[12].

There were a number of limitations to this study. First, our study sample size was insufficient to derive a common opinion on CV port systems among Turkish patients with cancer. The study was conducted only in our hospital and not all patients who received their chemotherapy via the port system agreed to participate in the survey. Since the survey was conducted with one-on-one interviews, it could be thought that patients with high satisfaction were more motivated to accept to participate in the survey. Finally, while creating our survey, we used the English version of a study originally written in Japanese. This might have caused semantic and expression problems during translations.

CONCLUSION

The vast majority of patients who received chemotherapy treatment through the CV port system were satisfied with this situation. They stated that their quality of life increased compared to the period in which peripheral vascular access was used. However, especially in our country, most of the patients still do not use CV ports. The fact that the existing fears and anxiety of the patients before the procedure cannot be elimi-

nated with adequate and correct information plays an important role in this. At this point, the operator (vascular surgeon, interventional radiologist, etc.) who performs the surgical procedure in the center where the procedure is performed should inform the patient and the nurses in the oncology and chemotherapy units who give the first information to the patient. Correct maintenance of the port system and training of the personnel on infection prophylaxis are very important after the procedure.

Ethics Committee Approval: The study was approved by Kartal Koşuyolu High Specialization Training and Research Hospital Non-Invasive Clinical Research Ethics Committee (Decision no: 2022/12/624, Date: 23.08.2022).

Informed Consent: Informed consent was obtained from all patients included in the exercise.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - İÇK; Analysis/Interpretation - İÇK; Data Collection - İÇK; Writing - İÇK; Critical Revision - İÇK; Statistical Analysis - İÇK; Overall Responsibility - İÇK.

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

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

REFERENCES

1. Moralar DG, Turkmen UA, Bilen A, Turkmen S, Feyizi H, Altan HA. Our central venous port catheter system practice-a retrospective study. J Pak Med Assoc 2021;71(5):1442-5.
2. Kesici S, Tuna V, Özkan S, Cengiz E, Türkmen A. Venöz port kateter implantasyonu uygulanan hastaların retrospektif analizi. Çukurova Med J 2017;42(3):604-5. [Crossref]
3. Tsuji Y, Tsushima T, Abe S, Tamura F, Mızushıma T, Nagashıma H, et al. A retrospective analysis of central venous access port in patients with malignancies. Jon J Clin 2008;58:675-80.
4. Taxbro K, Hammarskjöld F, Thelin B, Lewin F, Hagman H, Hanberger H, et al. Clinical impact of peripherally inserted central catheters vs implanted port catheters in patients with cancer: An open-label, randomised, two-centre trial. Br J Anaesth 2019;122(6):734-41. [Crossref]
5. Lipitz-Snyderman A, Elkin EB, Atoria CL, Sima CS, Epstein AS, Blinder V, et al. "Provider differences in use of implanted ports in older adults with cancer." Med Care 2015;53(7):646. [Crossref]
6. Madabhavi I, Patel A, Sarkar M, Anand A, Panchal H, Parikh S. "A study of use of "PORT" catheter in patients with cancer: A single-center experience." Clin Med Insights Oncol 2017;11:1-6. [Crossref]
7. Robinson A, Souied O, Bota A, Levasseur N, Stober C, Hilton J, et al. "Optimal vascular access strategies for patients receiving chemotherapy for early-stage breast cancer: A systematic review." Breast Cancer Res Treat 2018;171(3):607-20. [Crossref]
8. Yeşi˙lbalkan ÖU, Kir S, Karadakovan A, Uslu R. "Knowledge and attitudes of Turkish cancer patients regarding the implantable port catheter." Türk Onkoloji Derg 2009;24(3):108-14.
9. Nagel SN, Teichgräber UK, Kausche S, Lehmann A. Satisfaction and quality of life: A survey-based assessment in patients with a totally implantable venous port system. Eur J Cancer Care 2012;21:197-204. [Crossref]
10. Taxbro K, Berg S, Hammarskjöld F, Hanberger H, Malmvall BE. A prospective observational study on 249 subcutaneous central vein access ports in a Swedish country hospital. Acta Oncol 2013;52:893-901. [Crossref]
11. Vardy J, Engelhardt K, Cox K, Jacquet J, McDade A, Boyer M, et al. Long-term outcome of radiological-guided insertion of implanted central venous access port devices (CVAPD) for the delivery of chemotherapy in cancer patients: Institutional experience and review of the literature. Brit J Cancer 2004;91:1045-9. [Crossref]
12. Yagi T, Sakamoto T, Nakai K, Tanizawa M, Okabe T, Hoshikawa N, et al. "A questionnaire-based assessment of the anxiety, satisfaction and discomfort experienced by Japanese cancer patients during the use of central venous ports." Intern Med 2016;55(17):2393-9. [Crossref]

The Acute Effect of Fructose on Cardiac Hemodynamic Responses and Infarcted Area in Isolated Rat Heart During Ischemia-Reperfusion

Orkide Palabıyık[1](İD), Muhammed Ali Aydın[2](İD), Ecem Büşra Değer[2](İD), Selçuk Korkmaz[3](İD), Selma Arzu Vardar[2](İD)

[1] Department of Medical Services and Techniques, Trakya University Vocational School of Health Services, Edirne, Türkiye
[2] Department of Physiology, Trakya University Faculty of Medicine, Edirne, Türkiye
[3] Department of Biostatistics and Medical Informatics, Trakya University Faculty of Medicine, Edirne, Türkiye

ABSTRACT

Introduction: This study aimed to investigate the effects of fructose on cardiac hemodynamics and infarct size and the role of the antioxidant mechanism in these effects in isolated rat hearts undergoing ischemiareperfusion.

Patients and Methods: Isolated hearts obtained from female Wistar rats were perfused with Krebs-Henseleit solution containing 12 mM glucose or solution containing 12 mM fructose or 48 mM fructose and underwent lowflow ischemia followed by reperfusion on the Langendorff apparatus. Left ventricular developed pressure (LVDP), timedependent pressure changes (dp/dt max, dp/dt min) and heart rates were recorded at the 1st, 15th and 120th minutes of reperfusion following ischemia, and the percentage of the infarct area and the size of the risk area were determined. At the end of the reperfusion, total oxidant capacity (TOS), malondialdehyde (MDA) and glutathione (GSH) levels were examined in perfusion fluid samples.

Results: Basal dp/dt max values were lower in the high fructose group compared to the glucose group ($p= 0.032$). When the hearts were perfused with 12 mM fructose, a significant increase was observed in the percentage of the ischemic area and risk area compared to equivalent glucose and high fructose ($p< 0.001$ and $p< 0.001$, respectively). MDA, GSH and TOS values were comparable in all groups.

Conclusion: The present study shows that fructose perfusion plays a role in reduced ventricular contractile function relative to glucose in isolated rat hearts. This reduction triggered by fructose appears to be independent of antioxidant mechanisms. Furthermore, fructose perfusion at glucose-equivalent concentration causes a greater increase in infarct area in ischemic hearts, whereas an increase in fructose concentration appears to prevent this effect.

Key Words: Fructose; ischemia; reperfusion; heart

İzole Sıçan Kalbinde İskemi-Reperfüzyon Sırasında Fruktozun Kardiyak Hemodinamik Yanıtlara ve Enfarktüs Alanı Üzerine Akut Etkisi

ÖZET

Giriş: İskemi ve reperfüzyon uygulanan izole kalpte fruktozun kardiyak hemodinami, infarkt alanı büyüklüğü ve antioksidan hasara etkileri tam olarak bilinmemektedir. Çalışmada izole sıçan kalplerinde perfüzyon sıvısında uygulanan iki farklı konsantrasyondaki fruktozun kardiyak hemodinamik parametrelere, enfarktüs boyutuna etkisi ve bu etkilerde antioksidan mekanizmanın rolünün araştırılması amaçlanmıştır.

Hastalar ve Yöntem: Wistar albino türü ve 200-250 g ağırlığında 21 adet dişi sıçan kalbi anesteziyi takiben (100 mg/kg tiyopental, İP) Langendorff düzeneğine yerleştirildi. K grubunda kalpler 12 mM glukoz içeren Krebs-Henseleit (K/H) solüsyonuyla, F grubundaki kalpler glukoza eş değer 12 mM fruktoz ve YF grubundaki kalpler 48 mM yüksek fruktoz ile hazırlanmış solüsyonlarla deney boyunca perfüze edildi. Tüm gruplara 30 dk düşük akımlı iskemi (0.3 mL/dk) ve 120 dk reperfüzyon uygulandı. İnfarkt alan yüzdesi ve risk alanı boyutunu belirlemek için bilgisayarlı planimetri yöntemi kullanıldı. İskemi sonrası reperfüzyonun birinci, beşinci ve 120. dakikalarında sol ventrikül gelişim basıncı (SVGB), zamana bağlı basınç değişim değerleri (dp/dt maks, dp/dt min) ve kalp hızları kaydedildi. Reperfüzyonun sonunda perfüzyon sıvısı örneklerinde total oksidan kapasitesi (TOS), malondialdehit (MDA) ve glutatyon (GSH) düzeyleri incelendi. İstatistiksel karşılaştırmalarda tek yönlü varyans analizi, Kruskal Wallis testi ve Friedman testi kullanıldı.

Bulgular: İskemi öncesinde dp/dt maks değerleri, YF grubunda K grubuna göre anlamlı derecede düşük bulundu ($p= 0.032$). Kalpler 12 mM uygulanan fruktozla perfüze edildiğinde iskemik alan yüzdesi ve risk alanı değerlerinde eş değer düzeydeki glukoz ve yüksek fruktoza göre anlamlı artış görüldü (sırasıyla, $p< 0.001$, $p< 0.001$). MDA, GSH ve TOS değerleri tüm gruplarda benzerdi.

Cite this article as: *Palabıyık O, Aydın MA, Değer EB, Korkmaz S, Vardar SA. The acute effect of fructose on cardiac hemodynamic responses and infarcted area in isolated rat heart during ischemia-reperfusion. Koşuyolu Heart J 2023;26(1):7-13.*

Correspondence

Orkide Palabıyık

E-mail: orkide_69@hotmail.com
Submitted: 16.01.2023
Accepted: 04.03.2023
Available Online Date: 21.03.2023

Sonuç: Bu çalışma, izole sıçan kalbinde fruktoz perfüzyonun, glukoza göre ventrikül kasılma fonksiyonunu azaltıcı rol oynadığını göstermektedir. Fruktoza bağlı oluşan bu azalma, antioksidan mekanizmalardan bağımsız gibi görünmektedir. Ayrıca, glukoza eş değer konsatrasyonda fruktoz perfüzyonu, iskemik kalplerde infakt alanının daha fazla artışına sebep olmakta, fruktoz konsantrasyonundaki artış ise bu durumu önleyici gibi görünmektedir.

Anahtar Kelimeler: Fruktoz; iskemi; reperfüzyon; kalp

INTRODUCTION

Western-style diets of modern life and the widespread use of added sugars in the food industry have substantially increased the intake of fructose ($C_6H_{12}O_6$) in daily life. While approximately 1620 grams of fructose per day used to come from natural sources such as fruits, vegetables and honey in the past, the increasing consumption and availability of industrial food products has raised this amount up to 80150 g/day through the last fifty years[1]. It is suggested that the increase in fructose consumption is alarming and is in parallel with the increased prevalence of metabolic disorders (insulin resistance, metabolic syndrome, type 2 diabetes) and cardiovascular disease[2]. Although there has been major progress in cardiovascular diagnostics and therapeutics, myocardial infarction (MI) still remains a significant morbidity[3]. In this regard, cardiac infarction size is considered an important determinant of post-MI mortality[4]. Restoration of blood flow in the ischemic myocardium results in ischemia and/or reperfusion (I/R) injury. The length of ischemia is one of the primary factors associated with the recovery of cardiac function[5]. In this context, the resulting outcome is termed as cardiac muscle necrosis. For over 30 years, coronary reperfusion therapy has been used to manage myocardial infarction[5]. However, reperfusion itself following prolonged ischemia may lead to I/R injury. Clinical manifestations of such damage include angina, myocardial necrosis, arrhythmia, myocardial stunning, and endothelial dysfunction[6]. Although adenosine triphosphate (ATP) production in cardiomyocytes occurs through a mechanism that relies on fatty acid oxidation, ATP generated by means of glycolysis is also important[7]. Cardiac tissue is insulin-sensitive and dependent on glycolysis[7]. However, when glucose metabolism becomes insufficient or completely suppressed, fructose continues to be used in the glycolysis pathway. Cellular fructose intake is mediated by insulin-independent transporters. In this setting, the myocardium may be sensitive to the detrimental consequences of prolonged fructose intake[7,8].

Although numerous rodent studies have reported that a fructose-rich diet increases blood pressure[9], a great many studies investigating acute fructose ingestion in humans have not indicated increased sympathetic system activity, which is responsible for increased blood pressure[10]. There is no clear evidence from epidemiological studies linking fructose levels in common diets to risk factors for cardiovascular disease. There is only a limited number of experimental studies on this subject matter, and they have reported conflicting results. Some of the studies conducted to date have demonstrated harmful effects of fructose in the damage of myocardial reperfusion[11], while some others have shown a protective role[12,13]. In another study, we observed that fructose had a positive effect on the restoration of left ventricular contractile function after low-flow ischemia when a standard diet was compared to a high-fructose diet despite without any difference in the extent of myocardial infarction. Similar results were obtained in rats fed with fructose and glucose[14]. In addition, oxidative-destructive effects of dietary fructose intake, which suppress antioxidant defensive system and increase the free radical generation, have been demonstrated in rats[15]. In order to better understand the conflicting results reported in earlier studies and the acute cardiac effects of elevated fructose levels during ischemia-reperfusion, the present study aimed to investigate the effects of fructose on cardiac hemodynamic parameters, infarct size and oxidative changes when administered at two different concentrations, i.e. normal and high concentration in perfusion fluid to isolated rat hearts as well as comparing these effects against a control group administered with glucose.

PATIENTS and METHODS

Study Design

This study used 21 female Wistar albino rats weighing 200-250 g and raised under standard conditions (room temperature: 23 ± 1°C, humidity: 60%, 12/12 hours light/dark rhythm) at the Experimental Animals Unit of Trakya University. Rats were stratified into three groups as control (C), fructose (F), and high fructose (HF).

How the Krebs-Henseleit solution was prepared

Krebs-Henseleit (KH) solution was freshly prepared prior to each experiment. The solution (in mM) consisted of sodium chloride (NaCl= 118.5), sodium bicarbonate ($NaHCO_3$= 25), potassium chloride (KCl= 4.8), magnesium sulfate ($MgSO_4$= 1.2), D-glucose ($C_6H_{12}O_6$= 12), potassium dihydrogen phosphate (KH_2PO_4= 1.2), and calcium chloride ($CaCl_2$= 1.7). The hearts included in the control (C) group underwent perfusion with KH solution throughout the experiment. In the study, two different concentrations were used to investigate the cardiac effects of fructose. Group F received fructose instead of the glucose in the KH solution at the same amount of (12 mM).

Group HF received fructose instead of the glucose in the KH solution at a greater amount of (48 mM)[5]. All components were dissolved in distilled water. When adding components, calcium chloride was added after the others in order to prevent precipitation in the perfusion fluid.

Experiment protocol and hemodynamic measurements in isolated heart

All rats were administered 500 U/kg heparin (500 IU/kg: Nevparin Vial, Mustafa Nevzat İlaç Sanayi A.Ş., İstanbul, Türkiye) to prevent coagulation and 100 mg/kg thiopental (Ulagay A.Ş., İstanbul, Türkiye) for anesthesia by intraperitoneal injection[14]. Once anesthesia was induced, the hearts were swiftly excised, placed in Langendorff apparatus and perfused with KH solution previously equilibrated at 37ºC as 95% O_2/5% CO_2 (pH= 7.4). With the hearts placed in the apparatus, a balloon was inserted in the left ventricle to measure hemodynamic parameters.

Left ventricular developed pressure (LVDP= LV systolic pressure – LV diastolic pressure), time-dependent maximum contraction and relaxation values (dp/dt max, dp/dt min), aortic perfusion pressure and heart rate were recorded continuously in the hearts placed in Langendorff apparatus. For all isolated hearts, a 15-minute equilibration period followed by basal perfusion was performed at 15 minutes before ischemia. Basal perfusion was followed by 30 minutes of low-flow ischemia (0.3 mL/min) and 120 minutes of reperfusion (Figure 1)[5].

Evaluation of oxidative parameters

Total oxidant status (TOS), malondialdehyde (MDA) and glutathione (GSH) levels were measured to evaluate the oxidative state in the perfusion fluid collected at 120 minutes of reperfusion. TOS level was determined in line with the protocol recommended by the manufacturer using an ELISA kit (Rel Assay Diagnostic, Türkiye). Concentrations were measured with a spectrophotometer (Shimadzu UV-1700A-Japan) at 412 nm, and data were expressed in mmol H_2O_2 Eq/L[16]. MDA concentration in plasma, an indicator of lipid peroxidation, was analyzed according to the method described by Ohkawa, H et al.[17] using substances that react with thiobarbituric acid. These concentrations were measured spectrophotometrically at 512 nm, and data were expressed in mmol/L. After manual preparation, GSH values were determined by the method described by Ellman, GL et al[18]. GSH concentration was measured spectrophotometrically at 412 nm and the findings were expressed in ng/L.

Measuring the infarct area

After 120 minutes of reperfusion, all isolated hearts were wrapped in cling film and frozen at 20°C. Subsequently, left ventricular tissues were sliced into cross-sections of 12 mm thickness. To identify ischemic areas, these sections were incubated at 37°C in phosphate buffer containing 1% tetrazolium at pH= 7.4 for 15-20 minutes. Fixation was performed in 10% formalin solution. Following the staining process, the sections were dried using filter paper and transferred to a thin glass plate at a distance of 2 mm from each other. A second glass plate was placed over the sections and compressed with two clamps. Necrotic zone margins (tetrazoliumnegative tissue) and the risk zone were drawn on a transparent acetate placed on the glass. Mean of the risk zone/total area percentage (%) and risk area (mm^2) were calculated. All sections obtained from the heart slices were photographed. Necrotic areas were calculated using the computerized planimetric method[19].

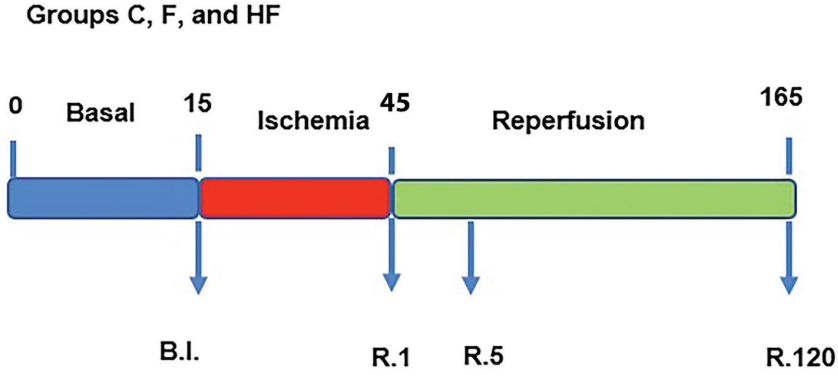

Figure 1. Applied ischemia reperfusion protocol: Fifteen minutes of perfusion, 30 minutes of low-flow ischemia (0.3 mL/min) and 120 minutes of reperfusion were applied to all hearts with appropriate perfusion fluid. The control (C) group was perfused with normal KH solution, the fructose group (F) was perfused with 12 mM fructose instead of glucose, and the hearts in the high fructose (HF) group were perfused with high fructose solutions containing 48 mM fructose instead of glucose. Minute 15 of the experiment, BI (basal measurement before ischemia), minute one (first minute of R1 Reperfusion), minute five (fifth minute of R5 Reperfusion), and minute 120 (120^{th} minute of R120 Reperfusion).

C: Control, F: Fructose, HF: High fructose.

Statistical Analysis

Normality assumption was checked using Shapiro-Wilk's test. Independent groups were compared using one-way ANOVA and Kruskall-Wallis test depending on normality. Dependent groups were compared using Friedman test. Pairwise comparisons were performed using Tukey and Dunn tests. A p-value less than 0.05 was considered statistically significant. All analyzes were conducted using TURCOSA (Turcosa Analytics Ltd Co, Türkiye, www.turcosa.com.tr) statistical software.

RESULTS

Evaluation of hemodynamic parameters during ischemia-reperfusion

In the present study, basal LVDP values before ischemia were similar in groups F and HF compared to group C (p= 0.077). No significant difference was observed between the groups in terms of LVDP levels during 120 minutes of reperfusion following 30 minutes of low-flow ischemia. However, the dp/dt max pressure change values recorded before ischemia were significantly lower in group HF compared to group C (p= 0.037). Before ischemia, dp/dt min and heart rate values at the measurement time points, R1, R5, and R120 during reperfusion were comparable across the three groups (Table 1).

Evaluation of oxidative state

Total oxidant status (TOS), malondialdehyde (MDA) and glutathione (GSH), which were explored to evaluate the oxidative state in perfusion fluid collected at 120 minutes of reperfusion, were not significantly different across the groups (p= 0.959, p= 0.574, p= 0.456, respectively) (Table 2).

Table 1. Hemodynamic values of the groups after ischemia-reperfusion

	C (n= 7)		F (n= 7)	HF (n= 7)	p
LVDP (mmHg)	**BI**	84 (66/102)	47 (14/64)	25 (3/60)	0.077
	R1	75 (19/98)	44 (11/109)	23 (6/116)	0.779
	R5	66 (28/105)	12 (1/50)	16 (5/75)	0.219
	R120	28 (22/30)	17 (1/48)	8 (6/18)	0.390
dp/dt max (mmHg)	**BI**	1293 (738/1642)	535 (141/-1002)	215 (-169/-486)*	0.037
	R1	1000 (192/1550)	175 (-276/-975)	-66 (-196/-1544)	0.309
	R5	882 (401/1957)	-127(-407/-506)	-76 (-208/-1004)	0.167
	R120	539 (274/621)	82 (-138/-408)	16 (-138/-154)	0.050
dp/dt min (mmHg)	**BI**	-1326 (-1660/ -990)	-711 (-1716/-261)	-465 (-691/-228)	0.117
	R1	-859 (-1057/ -207)	-995 (-1304/-239)	-447 (-1396/-329)	0.874
	R5	-988 (-1599/-391)	-567 (-1242/-131)	-281 (-431/-1179)	0.246
	R120	-418 (-426/-364)	-483 (-981/-123)	-221 (-553/-113)	0.584
HR (beat/min)	**BI**	228 (219/249)	216 (197/225)	231 (142/250)	0.551
	R1	166 (92/ 200)	113 (85/147)	113 (48/251)	0.694
	R5	253 (243/328)	191 (169/203)	92 (87/298)	0.116
	R120	224 (208/252)	140 (99/169)	141 (74/224)	0.077

(LVDP: Left ventricular developed pressure, time-dependent maximum contraction and relaxation values (dp/dt max, dp/dt min), HR: Heart rate (beat/minute), BI: Before ischemia, R1: First minute of reperfusion, R5: Fifth minute of reperfusion, R120: 120th minute of reperfusion, C: Control; F: Fructose; HF: High fructose.
(*p< 0.05 compared to the control group). Values are given as median (min/max).

Table 2. Oxidative parameters in the perfusion fluid

	C	F	HF	p
TOS (μmol H_2O_2 Eq/L)	2.41 ± 0.08	2.46 ± 0.08	2.38 ± 0.04	0.959
MDA (mmol/L)	7.25 ± 0.42	8.00 ± 0.54	8.10 ± 0.75	0.574
GSH (ng/L)	777.46 ± 55.39	724.10 ± 32.20	697.47 ± 44.57	0.456

TOS: Total oxidant status; MDA: Malondialdehyde; GSH: Glutathione; C: control; F: Fructose; HF: High fructose. N=7 in each group. Values are given as mean±SEM.

Table 3. Effects of fructose administration (12 and 48 mM) on myocardial infarct size in isolated rat hearts after 30 minutes of low-flow (0.3 mL/min) ischemia followed by 120 minutes of reperfusion

	C (n= 7)	F (n= 7)	HF (n= 7)	p
Infarcted volume $(mm)^3$	72.73 ± 5.43	108.63 ± 5.70***, #	80.50 ± 4.28	<0.001
Infarct size (%)	36.36 ± 2.68	54.33 ± 2.84***, #	40.275 ± 2.14	<0.001

Data are presented as mean ± SEM.
*** p< 0.001 compared to the control group.
#p< 0.01 compared to the HF group.
C: Control; F: Fructose; HF: High fructose.

Evaluation of infarct field

When the effects of fructose on infarct size as percentage and the infarct area in isolated rat hearts were examined, there was a statistically significant difference in mean infarcted myocardial volume (mm^3) between two different doses (12 and 48 mM) of fructose administered after 120 minutes of reperfusion following 30 minutes of low-flow (0.3 mL/min) ischemia (Table 3). The difference resulted from the fact that group F had higher results than both group C and group HF (p< 0.001 and p< 0.001, respectively). When the size of the infarct area was compared between the groups as the mean risk zone/total area percentage, a significant difference was found between the groups. This difference was driven by the higher percentage of infarct area in group F compared to group C and group HF (Table 3) and (Figure 2).

DISCUSSION

The increasing fructose consumption in recent years has been recognized as one of the factors causing cardiometabolic risk associated with obesity, diabetes and metabolic syndrome[20]. Acute MI, one of the leading cardiometabolic risks, is an important cause of mortality in the developed world[21].

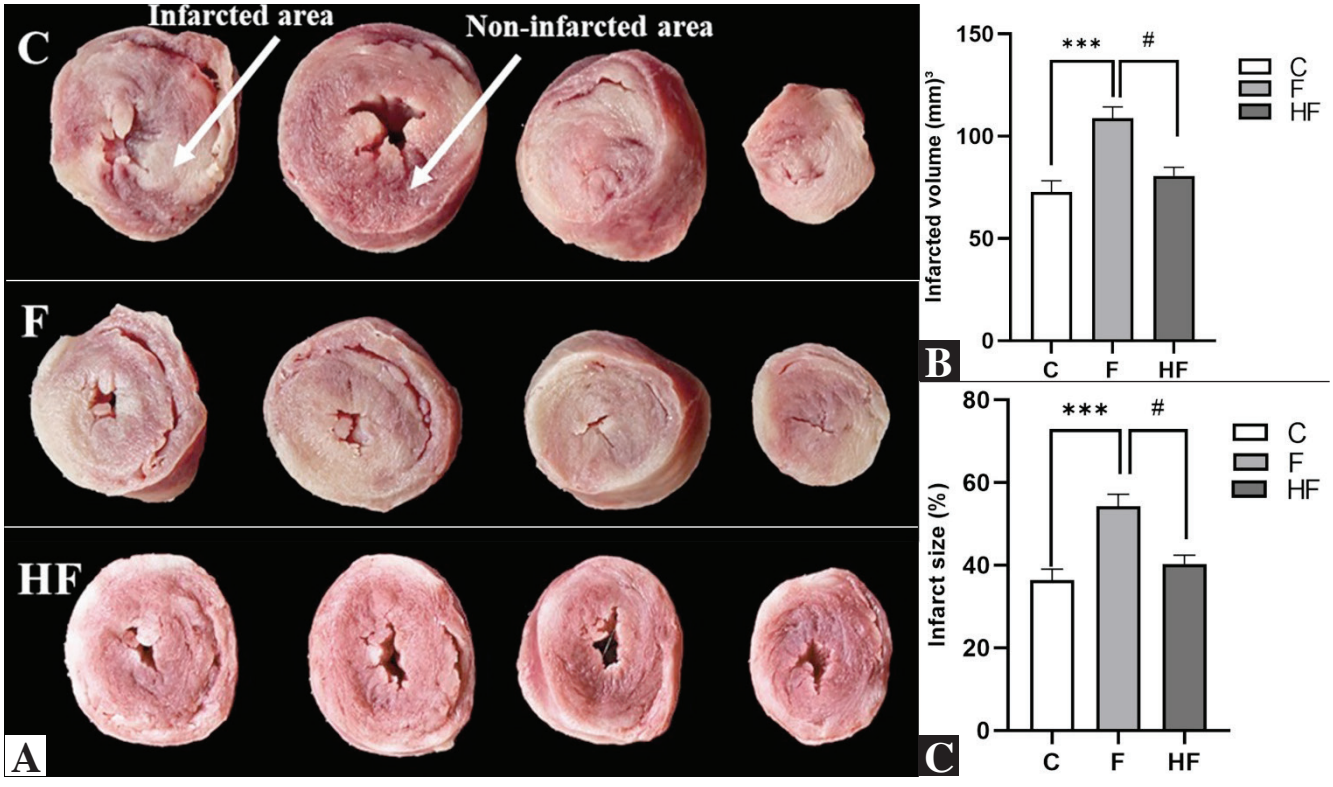

Figure 2. The effects caused by fructose administration on myocardial infarct volume and size in rat hearts after 30 minutes of low flow (0.3 mL/min) ischemia followed by 120 minutes of reperfusion. A: Representative heart sections from groups C, F and HF stained with tetrazolium chloride. Infarcted (dead-IA) and non-infarcted (live-N-IA) areas appear white (pale) and brick red, respectively. B: Infarcted volume (mm^3). C: Infarct size (%).

C: Control, F: Fructose (12 mM) and HF: High fructose (48 mM), KH: Krebs Henseleit solution.

(***: p< 0.001 compared to the control group, #: p< 0.001 compared to group HF).

The reperfusion period following ischemia may have a further lethal effect compared to the effect of ischemia, owing to calcium overload and generation of destructive free radicals. Currently, there are conflicting approaches to the effect of dietary fructose intake on cardiac ischemia. One of these approaches supports the notion that fructose has harmful effects in the damage caused by myocardial reperfusion[11], while the other supports that it may play a protective role in this setting[12].

In the present study, we aimed to investigate the effects caused by fructose at different concentrations on cardiac hemodynamic parameters and infarct size after low-flow I/R in isolated rat hearts. We used two different (i.e. normal and high) concentrations of fructose instead of the glucose administered in the KH solution and evaluated the effects. Our findings showed that high-concentration fructose reduced ventricular contractile function when administered under normal-flow perfusion conditions. We found a statistically significant decrease in dp/dt max levels in group HF (p= 0.032; Table 1). Supporting these findings, we observed that LVDP decreased to a level close to half when normal level of glucose-flow perfusion was applied for 15 minutes; however, the difference was not statistically significant (p= 0.077). Furthermore, the decrease in the dp/dt max level seen across the groups at the end of the reperfusion was close to a statistically significant difference. In addition, according to the findings of dp/dt min levels in this study, fructose did not cause a significant change on ventricular relaxation function.

In this study, we also determined that the administration of fructose at a concentration equivalent to glucose significantly increased the size and volume of the ischemic area. Our results suggest that fructose at a concentration equivalent to the glucose concentration used in the KH solution may not provide sufficient ATP for the normal functioning of the heart, leading to further necrosis and apoptosis of cardiomyocytes during ischemia followed by reperfusion. The findings of this study indicate that glucose has a more effective function than fructose as a source of carbohydrates in the nutrition of the heart muscle.

The effect of fructose on the ischemic area has not been fully elucidated. Contrary to our findings, a previous study, where three different concentrations of fructose have been administered instead of glucose, has reported that fructose reduces the percentage and size of the infarct area at all concentrations[5]. However, the same study has also shown that replacing the glucose used in the KH solution with fructose does not result in a significantly reduced number, shorter duration or less frequent occurrence of hazardous reperfusion arrhythmias, e.g. ventricular tachycardia and fibrillation[5]. Findings of an earlier study have indicated that preconditioning with fructose reduces the size of the infarct area as well as the arrhythmias triggered by ischemia and reperfusion[22]. The findings of our study showed that fructose reduced the percentage and size of the infarct area; however, with the limitation that we could not demonstrate a smaller number, shorter duration or reduced frequency of hazardous reperfusion arrhythmias.

Fructose metabolism is different from glucose metabolism, and the effects of fructose occur by means of an insulin-independent mechanism. Long-term dietary fructose intake may be detrimental for the myocardium as the heart is insulin-responsive[7]. A study in rats fed with a 66% fructose-enriched diet for four weeks has demonstrated decreased tolerance to local ischemia-reperfusion and an increase in infarct size[11]. However, the study by Jordan and colleagues, using a short-term (three-day) fructose-rich diet in rats, have reported that fructose has protective effects against myocardial ischemia/reperfusion injury[12] and as a possible cause of this situation, it has been suggested that dietary fructose intake may directly increase glycogen stores, leading to a higher level of anaerobic energy stored in the myocardium[12]. The data obtained in our study revealed an increase in ischemic area volume and percentage with low fructose concentration; however, the finding that infarct size in the high fructose group was similar to the control group supports this notion only partially. In another study, we have shown that high levels of dietary fructose intake for four weeks can produce favorable hemodynamic effects on left ventricular function without changing the size of myocardial infarct area during reperfusion after low-flow ischemia (0.3 mL/min) in hearts perfused with glucose-containing KH solution[14]. In terms of the factors affecting this finding, a previous study has reported that dietary fructose intake may also facilitate oxidative damage and has harmful effects due to a decrease in antioxidant defense as well as increased production of free radicals[23]. In the present study, TOS, MDA and GSH, which reflect the oxidative state in low-flow ischemia and reperfusion, were found to be similar in all groups.

CONCLUSION

In conclusion, the present study focused on the effects of fructose at different concentrations on cardiac hemodynamic parameters and infarct size after low-flow I/R in isolated rat hearts. At the two concentrations tested in the present study, fructose decreased ventricular contractile function both before low-flow ischemia and at the end of reperfusion while only low-concentration fructose administration increased the ischemic area. These results suggest that fructose at a concentration equivalent to that of glucose may not provide sufficient

ATP for the normal functioning of the heart, leading to necrosis and apoptosis of cardiomyocytes during ischemia/reperfusion. Further studies to elucidate the relevant mechanism may shed light on the acute effects caused by fructose in cardiac I/R.

Ethics Committee Approval: The approval for this study was obtained from Trakya University Local Ethics Committee of Animal Experiments (Decision no: 2021.05.05, Date: 28.05.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - OP, MAA, EBD, SAV; Analysis/Interpretation - OP, SAV, SK; Data Collection - OP, MAA, EBD; Writing - OP, SAV; Critical Revision - All of authors; Statistical Analysis -SK; Overall Responsibility - OP.

Conflict of Interest: The authors have no conflicts of interest to declare.

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

REFERENCES

1. Miller A, Adeli K. Dietary fructose and the metabolic syndrome. Curr Opin Gastroenterol 2008;24(2):204-9. [Crossref]
2. Bray G. Fructose: Should we worry? Int J Obesity 2008;32(7):127-31. [Crossref]
3. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Executive summary: Heart disease and stroke statistics-2010 update: Report from the American Heart Association. Circulation 2010;121(7):948-54. [Crossref]
4. Shah SR, Hochberg CP, Pinto DS, Gibson CM. Reperfusion strategies for ST-elevation myocardial infarction. Curr Cardiol Rep 2007;9(4):281-8. [Crossref]
5. Haghi J, Eteraf-Oskouei T, Najafi M. Effects of postconditioning with fructose on arrhythmias and the size of infarct caused by global ischemia and reperfusion in isolated rat heart. Adv Pharm Bull 2018;8(1):57. [Crossref]
6. Wang J, Li J. Activated protein C: A potential cardioprotective factor against ischemic injury during ischemia/reperfusion. Am J Transl Res 2009;1(4):381.
7. Mellor KM, Bell JR, Wendt IR, Davidoff AJ, Ritchie RH, Delbridge LM. Fructose modulates cardiomyocyte excitation-contraction coupling and Ca2+ handling in vitro. PLoS One 2011;6(9):e25204. [Crossref]
8. Moens A, Claeys M, Timmermans J, Vrints C. Myocardial ischemia/reperfusion-injury, a clinical view on a complex pathophysiological process. Int J Cardiol 2005;100(2):179-90. [Crossref]
9. Tappy L, Lê KA. Metabolic effects of fructose and the worldwide increase in obesity. Physiol Rev 2010;90(1):23-46. [Crossref]
10. Cha SH, Wolfgang M, Tokutake Y, Chohnan S, Lane MD. Differential effects of central fructose and glucose on hypothalamic malonyl-CoA and food intake. Proc Natl Acad Sci USA 2008;105(44):16871-5. [Crossref]
11. Morel S, Berthonneche C, Tanguy S, Toufektsian MC, Foulon T, De Lorgeril M, et al. Insulin resistance modifies plasma fatty acid distribution and decreases cardiac tolerance to in vivo ischaemia/reperfusion in rats. Clin Exp Pharmacol Physiol. 2003;30(7):446-51. [Crossref]
12. Jordan JE, Simandle SA, Tulbert CD, Busija DW, Miller AW. Fructose-fed rats are protected against ischemia/reperfusion injury. J Pharmacol Exp Ther 2003;307(3):1007-11. [Crossref]
13. Faure MJ, Rossini E, Ribuot C, Faure P. Fructose-fed rat hearts are protected against ischemia-reperfusion injury. Exp Biol Med 2006;231(4):456-62. [Crossref]
14. Özen ST, Palabiyik O, Guksu Z, Arslan E, Tosunoğlu EA, Necdet S, et al. The effect of high-fructose feeding on hemodynamic behavior and infarct size of isolated rat hearts subjected to low-flow ischemia. Genel Tıp Dergisi 32(3):324-9.
15. Nandhini A, Thirunavukkarasu V, Ravichandran M, Anuradha C. Effect of taurine on biomarkers of oxidative stress in tissues of fructose-fed insulin-resistant rats. Singapore Med J 2005;46(2):82.
16. Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem 2005;38(12):1103-11. [Crossref]
17. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by t hiobarbituric acid reaction. Anal Biochem 1979;95(2):351-8. https://doi.org/10.1016/0003-2697(79)90738-3 [Crossref]
18. Ellman GL. Tissue sulfhydryl groups. Arch Biochem Biophys 1959;82(1):70-7. [Crossref]
19. Sahna E, Acet A, Kaya Ozer M, Olmez E. Myocardial ischemia-reperfusion in rats: Reduction of infarct size by either supplemental physiological or pharmacological doses of melatonin. J Pineal Res 2002;33(4):234-8. [Crossref]
20. Herman MA, Birnbaum MJ. Molecular aspects of fructose metabolism and metabolic disease. Cell Metabolism 2021;33(12):2329-54. [Crossref]
21. Parlakpinar H, Orum M, Sagir M. Pathophysiology of myocardial ischemia reperfusion injury: A review. Med Sci 2013;2(4):935-54. [Crossref]
22. Azari MH, Najafi M. Role of fructose as a potent antiarrhythmic and anti-infarct agent in isolated rat heart. Iranian J Pharm Res 2014;13(4):1303.
23. Busserolles J, Gueux E, Rock E, Mazur A, Rayssiguier Y. Substituting honey for refined carbohydrates protects rats from hypertriglyceridemic and prooxidative effects of fructose. J Nutr 2002;132(11):3379-82. [Crossref]

 ● Koşuyolu Heart J 2023;26(1):14-19 • DOI: 10.51645/khj.20239903

Clinical Characteristics and in-Hospital Outcomes of Patients Undergoing Left Atrial Appendage Closure

Gönül Zeren[1](İD), Fatma Can[1](İD), Mustafa Azmi Sungur[1](İD), Şahin Yılmaz[2](İD), Can Yücel Karabay[1](İD)

[1] Clinic of Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Türkiye
[2] Clinic of Anaesthesiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Introduction: Percutaneous left atrial appendage closure (LAAC) is considered in patients with non-valvular atrial fibrillation (AF) who cannot receive long-term anticoagulant therapy or who experience thromboembolism despite anticoagulant therapy. The structural feature of the left atrial appendage (LAA) and high variability of the clinical features of the patients endorse the difficulty of the procedure. In this study, it was aimed to present our single-center LAAC experience and in-hospital follow-up results of the patients.

Patients and Methods: Patients who had undergone LAAC in our cardiology clinic between 2017 and 2022 were included in the study retrospectively. All clinical, laboratory and imaging characteristics of the patients and in-hospital follow-up results were evaluated.

Results: Median age of 29 patients included in the study was 78 years (65-82, IQR= 25-75) and 17 were males (58.6%). Median score of CHA_2DS_2-VASc was 4 (4-6, IQR= 25-75). In addition, median value of the HAS-BLED score was 3 (3-4, IQR= 25-75). The rate of complete closure, minor bleeding during the procedure, and pericardial tamponade were 27 (93.1%), 1 (3.4%), and 1 (3.4%) respectively, and the device was dislocated immediately after the procedure in one patient (3.4%). The most common type of LAA appendix was chicken wings 15 (51.7%).

Conclusion: Success rate of the LAAC procedure was high in this single-center study conducted in our country with a relatively high number of patients.

Key Words: Atrial fibrillation; anticoagulant drugs; thromboembolism

Sol Atriyal Apendiks Kapatma Yapılan Hastaların Klinik Özellikleri ve Hastane İçi Sonlanımları

ÖZET

Giriş: Non-valvüler atriyal fibrilasyonu (AF) olan, uzun süreli antikoagülan tedavi alamayan ya da antikoagülan tedaviye rağmen tromboemboli geçiren olgularda, perkütan sol atriyal apendiks kapatma (SAAK) düşünülmektedir. Sol atriyal apendiksin (SAA) yapısal özelliği ile hastaların klinik özelliklerinin yüksek değişkenliği, prosedürün zorluğunu desteklemektedir. Biz bu çalışmada, tek merkezli SAAK deneyimimizi ve hastaların hastane içi takip sonuçlarını vermeyi amaçladık.

Hastalar ve Yöntem: Çalışmamıza kardiyoloji kliniğimizde 2017-2022 yılları arasında SAAK yapılan hastalar retrospektif olarak alındı. Hastaların tüm klinik, laboratuvar ve görüntüleme özellikleri ve hastane içi takip sonuçları değerlendirildi.

Bulgular: Çalışmaya dahil edilen toplam 29 hastanın yaş ortalaması 78 (65-82, IQR= 25-75) ve çoğunluğu erkek (%58.6) idi. CHA_2DS_2-VASc'nin medyan skoru 4 (4-6, IQR= 25-75) idi. Ayrıca HAS-BLED skorunun ortanca değeri 3 (3-4, IQR= 25-75) idi. İşlem sırasında tam kapanma, küçük kanama ve perikardiyal tamponad oranı sırasıyla 27 (%93.1), 1 (%3.4) ve 1 (%3.4) idi ve bir hastada işlemden hemen sonra cihaz yerinden çıktı (%3.4). SAA'nin en sık görülen tipi tavuk kanadı idi (%51.7).

Sonuç: Ülkemizde yapılan, tek merkezli, nispeten yüksek hasta sayısına sahip bu çalışmada, LAAK işleminin başarı oranı yüksektir.

Anahtar Kelimeler: Atriyal fibrilasyon; antikoagülan ilaçlar; tromboembolizm

Cite this article as: *Zeren G, Can F, Sungur MA, Yılmaz Ş, Karabay CY. Clinical characteristics and in-hospital outcomes of patients undergoing left atrial appendage closure Koşuyolu Heart J 2023;26(1):14-19.*

Correspondence

Gönül Zeren

E-mail: gonulzeren@hotmail.com
Submitted: 13.10.2022
Accepted: 12.12.2022
Available Online Date: 21.03.2023

INTRODUCTION

Atrial fibrillation (AF) is an important cause of mortality and morbidity due to increased risk of ischemic stroke. It is responsible for approximately 20-30% of all ischemic strokes[1-3]. Oral anticoagulant therapy, both vitamin K antagonist (VKA) and non-vitamin K antagonist oral anticoagulants (NOAC) are the only drugs to prevent ischemic stroke due to AF[2,4]. However, the use of anticoagulants may pose a safety risk, especially in patients who are elderly, have liver and renal dysfunction, have a high risk of bleeding due to use of other drugs and have a history of bleeding under anticoagulant therapy[5,6]. In cases where the HAS-BLED risk score, which is frequently used to evaluate individual bleeding risk, is 3 and above, the annual risk of major bleeding is around 5.8%[2].

Due to its general structure and characteristics, LAA is often the source of left atrial thromboembolism due to AF and is responsible for >90% of it[7]. For this reason, LAAC procedure has become widespread with increasing experience and technological developments in high-risk patients for whom OAC use is contraindicated or who develop thromboembolism under OAC. Short and long-term positive results have been supported by many randomized controlled studies[8-11].

In this study, it was aimed to present our LAAC experience in our single-center clinic, clinical, laboratory and imaging characteristics of our patients and in-hospital follow-up results.

PATIENTS and METHODS

Patients who had undergone LAAC in our clinic between 2017 and 2022 were included in study retrospectively. An informed consent form was obtained from all patients before the procedure. All clinical, laboratory and imaging characteristics of the patients and in-hospital follow-up results were evaluated. Ethics committee approval for the study was obtained from Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (Ethics Committee No: HNEAH-KAEK 2022/34).

Procedure

Following percutaneous puncture of the femoral vein, left atrial access is gained by transseptal puncture, ideally in the infero-posterior part of the interatrial septum. Thereafter, a device-specific sheath is introduced to the LA over a stiff guidewire, which is either placed in the left upper pulmonary vein or in LA. LAA angiogram is performed through the delivery sheath or via a pigtail catheter in right anterior oblique caudal and cranial projections and, less importantly, left anterior oblique or lateral projections. LAA dimensions of the ostium, the neck, i.e., the landing-zone and depth are measured or estimated to help choose the appropriate occluder type and size. The occluder is advanced through the delivery sheath and positioned into the LAA. Its position is confirmed via fluoroscopy, transesophageal echocardiography (TEE), and a tug test is performed. Finally, the occluder is released.

In our center, closure was performed using TEE before and during the procedure, under deep sedation and general anesthesia, considering the patient's comorbidity. In all groups, intraprocedural monitoring included continuous invasive measurement of the arterial blood pressure via a radial artery catheter. Continuous ECG monitoring and pulse oximetry for transcutaneous arterial oxygen saturation were performed. All patients were followed up in the intensive care unit after procedure until they were awake and hemodynamic stability was achieved.

Definitions

CHA_2DS_2-VASc: CHA_2DS_2-VASc score as previously described: 2 points each were assigned for age ≥75 years (A_2) and for history of stroke, TIA, or thromboembolism (S_2) and 1 point was assigned for each of the following items including congestive heart failure (C), hypertension (H), diabetes mellitus (D), age 65-75 years (A), vascular disease (VA) (defined as previous myocardial infarction, complex aortic plaque, carotid stenosis, and peripheral artery disease) and female sex category (Sc)[12,13].

HAS-BLED: HAS-BLED score as previously described: 1 point each were assigned for hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (n> 65), and drugs/alcohol concomitantly[7].

High bleeding risk: A score of "≥3" according to the HAS-BLED score recognized as high bleeding risk.

Classification of LAA morphology: The chicken wing LAA, with an obvious bend in the proximal or middle part of the dominant lobe or folding back of the LAA anatomy on itself at some distance from the perceived LAA ostium. This type of LAA may have secondary lobes or twigs. The windsock LAA, with one dominant lobe of sufficient length as the primary structure. Variations of this LAA type arise with the location and number of secondary or even tertiary lobes arising from the dominant lobe. The cactus LAA, with a dominant central lobe with secondary lobes extending from the central lobe in both superior and inferior directions. The cauliflower LAA, with limited overall length with more complex internal characteristics. Variations of this LAA type have a more irregular shape of the LAA ostium (oval vs. round) and a variable number of lobes with lack of a dominant lobe. The "cauliflower" morphology is most often associated with an embolic event[14].

Statistical Analysis

Continuous variables are presented as median and interquartile range (IQR). Categorical variables are presented as numbers and percentages. All statistical analyzes were performed with R version 4.0.4 (Vienna, Austria) using the "Hmisc" and "ggplot2" packages.

RESULTS

Median age of 29 patients included in the study was 78 years (65-82, IQR= 25-75), and 17 were males (58.6%). Median score of CHA_2DS_2-VASc was 4 (4-6, IQR= 25-75). In addition, median value of the HAS-BLED score was 3 (3-4, IQR= 25-75). All demographic and clinical findings of the patients are summarized in Table 1. In Figure 1, the histogram of HAS-BLED and CHA_2DS_2-VASc scores of all patients is presented.

Eight of the patients (27.5%) had pre-implantation spontaneous echo contrast (SEC), and eight (27.6%) had pre-procedural NOAC use. The rate of complete closure, minor bleeding during the procedure, and pericardial tamponade were 27 (93.1%), one (3.4%), and one (3.4%) respectively, and the device was dislocated immediately after the procedure in one patient (3.4%). The most common type of LAA appendix was chicken wings found in 15 patients (51.7%). All procedural and imaging characteristics of the patients are given in Table 2.

DISCUSSION

In high-risk patients who cannot receive oral anticoagulant therapy, who experience bleeding and thromboembolism during treatment, LAAC is a treatment option with a high success rate and predictable complication rate.

In the first randomized controlled PROTECT-AF trial on LAA closure devices, the Watchman (Boston Scientific Co., USA) device has been used, and it has been shown that LAA closure with the device was non-inferior to warfarin in preventing cerebrovascular events[8]. In the follow-up with another comprehensive randomized PREVAIL trial, it has also been observed that procedural safety was improved with less complication rate[9]. Five-year follow-up results of both trials have also been published; Watchman has shown that LAAC, non-inferior to warfarin, provides stroke prevention in nonvalvular atrial fibrillation and additional reductions especially in major bleeding, hemorrhagic stroke, and death[10]. In another recently published randomized controlled AMULET-IDE trial, it has been shown that for non-valvular atrial fibrillation, the Amulet (Abbott Vascular, USA) device was non-inferior to the Watchman device in terms of safety and effectiveness, and superior in terms of complete occlusion of the LAA. It has been observed that procedural complications were relatively higher in the Amulet group; however, it was decreased with operator experience. The most common procedural complications have been shown to be pericardial effusion and device embolization[11]. In recent years, due to increase in operator

Table 1. Baseline clinical and laboratory characteristics

Variables	Overall group (n= 29)
Age (years)	78 (65-82)
Sex (male)	17 (58.6)
Hypertension	28 (96.6)
Diabetes mellitus	17 (58.6)
Hyperlipidemia	12 (41.4)
Smoke	5 (17.2)
COPD	4 (13.8)
Congestive heart failure	12 (41.4)
Body mass index (kg/m^2)	27 (22-29)
NYHA class	
1	15 (51.7)
2	10 (34.5)
3-4	4 (13.8)
Coronary artery disease	19 (65.5)
Prior PCI	9 (31)
CABG	7 (24.1)
Prior TIA	2 (6.9)
Prior stroke	6 (20.7)
GFR ($mL/min/1.73\ m^2$)	59.3 (23.9-73.1)
Hemoglobin (g/dL)	10.5 (9.8-12.1)
CHA_2DS_2VASc score	4 (4-6)
HAS-BLED score	3 (3-4)
Albumin (g/dL)	3.5 (3-3.9)
Neutrophil ($\times10^3/\mu L$)	4.6 (3.3-5.9)
Lymphocyte ($\times10^3/\mu L$)	1.1 (0.9-1.7)
ALT (IU/L)	14 (11-19)
AST (IU/L)	17 (12-25)
Total cholesterol (mg/dL)	163 (132-199)

Categorical data are presented as numbers (percentages) and continuous data are presented as median (interquartile range).

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CABG: Coronary artery bypass grafting, CHA_2DS_2VASC: Congestive heart failure, hypertension, age, diabetes mellitus, stroke, vascular diseases, sex category, COPD: Chronic obstructive pulmonary disease, GFR: Glomerular filtration rate, HAS-BLED: Hypertension, abnormal renal/liver function, stroke, bleeding history, labile international normalized ratio or INR, elderly >65 years, drugs/alcohol, NYHA: New York Heart Association, PCI: Percutaneous coronary intervention, TIA: Transient ischaemic attack.

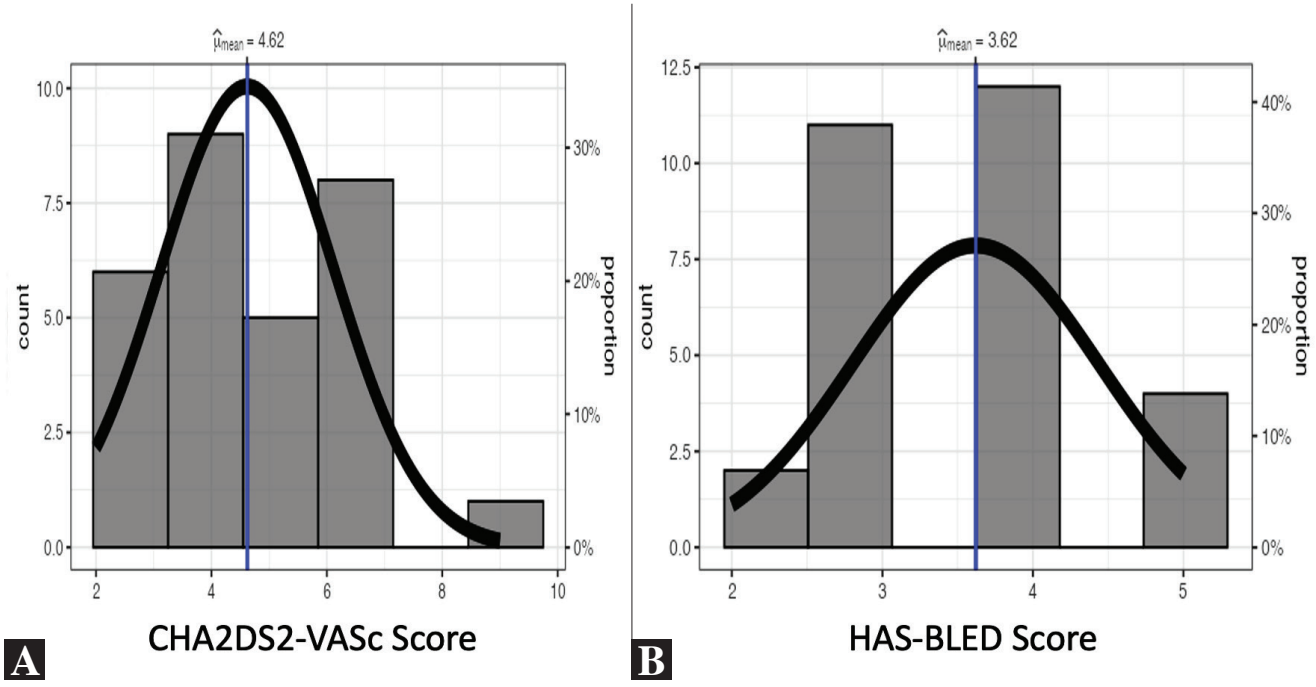

Figure 1. The histogram of HAS-BLED and CHA2DS2-VASc scores of all patients.

experience and the development of device features, the success rates of the procedure in LAAC have increased and the complication rates have been reduced. We had a high procedural success rate (93.1%) in our LAAC patients, in which we used the Amulet device. While device implantation success rate has been found as 90.9% in the PROTECT-AF study, the PREVAIL study has shown a 95.1% implantation success rate with new operators, similar to our study[8-10]. In the literature, it has been shown that pericardial effusions requiring surgical repair or pericardiocentesis decrease with increasing operator experience[8-11]. Pericardial effusion was seen in only one patient in our study, and device dislocation was also seen in one patient. A difference of our study to PROTECT-AF and PREVAIL studies is that the median CHA2DS2-VASc score was 4 compared to 2.2 in PROTECT-AF and to 2.6 in PREVAIL. However, CHA2DS2-VASc and HAS-BLED scores were similar to AMULET IDE (4.5 and 3.2, respectively)[8-11].

Since LAAC is a preventative treatment, it is extremely important to keep periprocedural complications low. Due to the heterogeneous anatomy of LAA, the procedure can be challenging. The success and complication of the procedure depend on several factors, such as patient characteristics and comorbidities, operator experience and device specifications. Good cardiac imaging is essential to evaluate LAA thrombus and its anatomical structure before the procedure and to ensure correct positioning of the device during the procedure. For this purpose, TEE, computed tomography (CT) is usually performed before the procedure, as well as TEE or intracardiac echocardiography during the procedure.

In nonvalvular AF, >90% of left atrial thrombi are found in LAA[7]. LAA is a tube-shaped blind sac with a volume of 5-15 mL extending from the main body of the atrium. It often has an oval-shaped mouth, and its inner surface is trabeculated by pectinate muscles. It can be a single-lobed and often more than one-lobed structure. Thrombus formation in this region is common during AF due to both atrial contractility, stasis and hypercoagulation, and the structure of LAA. In the literature, LAA has been classified into four main types according to its morphological structure[14]. These include chicken wing, windsock, cactus, and cauliflower, and the most common type is chicken wing. LAA morphology has been shown to affect the risk of thromboembolic events. Stroke or transient ischemic attack (TIA) is more common in the cauliflower type than in the chicken wing or windsock type. The morphological diversity of LAA also affects the success and complication rates of the interventional procedure. Chicken wing type LAA was observed in 51.7% of our patients.

Study Limitations

This study had several limitations. Although it was one of the centers where the most LAAC procedures were performed in the country during the study period, the number of patients in the study was small. Since the outcomes in our study were few, the results should be evaluated carefully. The retrospective design of the study was another important limitation.

Table 2. Procedural and imaging characteristics

Variables	Overall group (n= 29)
LAA SEC	8 (27.5)
NOAC use	8 (27.6)
Warfarin use	12 (41.4)
Antiplatelet use	17 (58.6)
Reason of implantation	
GIS bleeding	8 (27.6)
Intracranial bleeding	3 (10.3)
High bleeding risk (no event)	8 (27.6)
High bleeding risk (event)	2 (6.9)
Recurrent bleeding	6 (20.7)
Poor drug compliance	1 (3.4)
Repeated CVA	1 (3.4)
Complete closure (non/or <3 mm)	27 (93.1)
Minor bleeding	1 (3.4)
Immediate device dislocation	1 (3.4)
Pericardial effusion	1 (3.4)
LAA length (mm)	22 (19-25)
LAA ostium (mm)	19 (18-22.5)
Landing zone (mm)	16 (14-17)
Device size (mm)	25 (25-28)
LAA anatomy	
Chicken wing	15 (51.7)
Windsock	8 (27.6)
Cactus	4 (13.8)
Cauliflower	2 (6.9)

Categorical data are presented as numbers (percentages) and continuous data are presented as median (interquartile range).

CVA: Cerebrovascular accident, GIS: Gastrointestinal system, LAA: Left atrial appendage, NOAC: Non-vitamin K antagonist, SEC: Spontaneous echo contrast.

CONCLUSION

The success rate of the LAAC procedure is high in this single-center study conducted in our country with a relatively high number of patients. LAAC should be kept in mind as an alternative treatment in patients with nonvalvular atrial fibrillation (AF), who cannot receive long-term anticoagulant therapy, or who develop thromboembolism despite anticoagulant therapy.

Ethics Committee Approval: The study was approved by the ethics committee of Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (Decision no: HNEAH-KAEK 2022/34, Date: 21.02.2022).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design – GZ, CYK; Analysis/Interpretation – GZ, CYK; Data Collection - FC, ŞY; Writing – GZ, FC; Critical Revision – GZ, CYK, MAS; Final Approval - MAS; Statistical Analysis – CYK, MAS.

Conflict of Interest: The authors have no conflicts of interest to declare.

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

REFERENCES

1. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation 2014;130(23):199-267. [Crossref]
2. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37(38):2893-962. [Crossref]
3. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics-2019 update: A report from the American Heart Association. Circulation 2019;139(10): e56-528.
4. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland Jr JC, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. Circulation 2019;140(2):125-51. [Crossref]
5. Hylek EM, D'Antonio J, Evans-Molina C, Shea C, Henault LE, Regan S. Translating the results of randomized trials into clinical practice: The challenge of warfarin candidacy among hospitalized elderly patients with atrial fibrillation. Stroke 2006;37(4):1075-80. [Crossref]
6. Kuno T, Takagi H, Ando T, Sugiyama T, Miyashita S, Valentin N, et al. Oral anticoagulation for patients with atrial fibrillation on long- term hemodialysis. J Am Coll Cardiol 2020;75(3):273-85. [Crossref]
7. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: The Euro Heart Survey. Chest 2010;138(5):1093-100. [Crossref]
8. Reddy VY, Sievert H, Halperin J, Doshi SK, Buchbinder M, Neuzil P, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: A randomized clinical trial. JAMA 2014;312(19):1988-98. [Crossref]
9. Holmes DR Jr, Kar S, Price MJ, Whisenant B, Sievert H, Doshi SK, et al. Prospective randomized evaluation of the Watchman left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy: The PREVAIL trial. J Am Coll Cardiol 2014;64(1):1-12. [Crossref]
10. Reddy VY, Doshi SK, Kar S, Gibson DN, Price MJ, Huber K, et al.; PREVAIL and PROTECT AF Investigators. 5-year outcomes after left atrial appendage closure: From the PREVAIL and PROTECT AF trials. J Am Coll Cardiol 2017;70:2964-75. [Crossref]

11. Lakkireddy D, Thaler D, Ellis CR, Swarup V, Sondergaard L, Carroll J, et al. Amplatzer amulet left atrial appendage occluder versus watchman device for stroke prophylaxis (Amulet IDE): A randomized, controlled trial. Circulation 2021;144(19):1543-52. **[Crossref]**

12. Camm AJ, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation. Euro Heart J 2010;31:2369-429. **[Crossref]**

13. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor based approach: The Euro Heart survey on atrial fibrillation. Chest 2010;137:263-72. **[Crossref]**

14. Di Biase L, Santangeli P, Anselmino M, Mohanty P, Salvetti I, Gili S, et al. Does the left atrial appendage morphology correlate with the risk of stroke in patients with atrial fibrillation? Results from a multicenter study. J Am Coll Cardiol 2012;60:531-8. **[Crossref]**

Comparison of the Performance of Five Different Scoring Systems in Patients with ST-Elevation Myocardial Infarction

Flora Özkalaycı Kaçar[1](İD), Mehmet Saygı[1](İD), Tanıl Özer[2](İD), Ali Karagöz[2](İD), İbrahim Halil Tanboğa[3](İD), Vecih Oduncu[4](İD)

[1] Clinic of Cardiology, Hisar Intercontinental Hospital, İstanbul, Türkiye
[2] Clinic of Cardiology, Kartal Koşuyolu Training and Research Hospital, İstanbul, Türkiye
[3] Department of Biostatistics and Cardiology, Nişantaşı University Faculty of Medicine, İstanbul, Türkiye
[4] Department of Cardiology, Bahçeşehir University Faculty of Medicine, İstanbul, Türkiye

ABSTRACT

Introduction: Although most of the scoring systems are used for long-term mortality assessment in ST-elevation myocardial infarction (STEMI), there is still lack of data comparing model performances. In this study, it was aimed to compare five scoring systems for predicting long-term mortality in patients presented with STEMI.

Patients and Methods: This is a retrospective observational study consisting of 1689 consecutive STEMI patients who underwent PCI between 2009 and 2013. Patient data was obtained from the electronic data base of the hospital. Each patients' mortality risk was assessed with five different risk scores and recorded.

Results: A total of 1689 patients with STEMI were included into the study. Median follow-up time was one year. Risk scores were calculated for each patient. Although similar statistical significance was presented among all scores, modified age, creatinine clearance, and ejection fraction score (mACEF) were demonstrated to be more significant than relevant scoring systems in clinical respect.

Conclusion: Among five scores, the mACEF score was demonstrated to be the most significant model in clinical respect for the prediction of mortality.

Key Words: ST-elevation myocardial infarction; mortality; risk score

ST Elevasyonlu Miyaokard Enfarktüsü Geçiren Hastalarda Beş Farklı Skorlama Sisteminin Karşılaştırılması

ÖZET

Giriş: ST elevasyonlu miyokard enfarktüsünde (STEMI) uzun vadeli mortalitenin değerlendirmesinde çeşitli skorlama sistemleri kullanılmaktadır. Buna rağmen bu skorlama sistemlerinin performanslarını değerlendiren çalışmalar kısıtlı sayıdadır. Bu çalışmada STEMI ile başvuran hastalarda uzun dönem mortaliteyi öngörmek için beş skorlama sistemini karşılaştırmayı amaçladık.

Hastalar ve Yöntem: 2009-2013 yılları arasında perkütan koroner girişim yapılan ardışık 1689 STEMI hastası retrospektif olarak incelendi. Hasta verileri hastanenin elektronik veri tabanından elde edildi. Her hastanın mortalite riski beş farklı risk skoru ile değerlendirildi ve kaydedildi.

Bulgular: Çalışmaya toplam 1689 STEMI hastası dahil edildi. Medyan takip süresi bir yıldı. Her hasta için risk skorları hesaplandı. Tüm skorlar arasında benzer istatistiksel anlamlılık sunulmasına rağmen, modifiye yaş, kreatinin klirensi ve ejeksiyon fraksiyon skorunun (mACEF) ilgili skorlama sistemlerinden klinik açıdan daha anlamlı olduğu gösterilmiştir.

Sonuç: Beş skor arasında, mACEF skorunun mortaliteyi öngörmede klinik açıdan en anlamlı model olduğu gösterildi.

Anahtar Kelimeler: ST-elevasyonlu miyokard infarktüs; mortalite; risk skoru

INTRODUCTION

Coronary artery disease (CAD) is a well-known cause of mortality worldwide[(1)]. In this context, short- and long-term management of STEMI is extremely important.

Guidelines are provided in terms of managing these patients[(2)]. Despite all appropriate treatment strategies, mortality risk remains in the long-term follow-up.

Cite this article as: Özkalaycı Kaçar F, Saygı M, Özer T, Karagöz A, Tanboğa İH, Oduncu V. Comparison of the performance of five different scoring systems in patients with ST-elevation myocardial infarction. Koşuyolu Heart J 2023;26(1):20-26.

Correspondence

Flora Özkalaycı Kaçar

E-mail: florataniel@yahoo.com
Submitted: 23.09.2022
Accepted: 05.12.2022
Available Online Date: 21.03.2023

Several risk scoring systems have been developed to predict short- and long-term mortality risk in patients with STEMI. It is vital to apply appropriate treatment modalities to patients presented with acute coronary syndromes. Thrombolysis in myocardial infarction (TIMI) score was developed for the assessment of risk of death and ischemic events in patients with non-STEMI and unstable angina. Likewise, TIMI risk index (TRI) has been developed to predict the risk of mortality at 30 days in patients treated with fibrinolytics and later validated for STEMI patients undergoing pPCI for predicting one-year mortality[3-5].

The primary angioplasty in myocardial infarction (PAMI) risk score has been developed for predicting mortality in six-months in patients underwent PCI. Likewise, the controlled abciximab and device investigation to lower late angioplasty complications (CADILLAC) risk score has originally been developed for the prediction of one-year mortality in patients undergoing invasive procedures[6,7]. Thrombolysis in myocardial infarction risk index has been developed as a simple tool for predicting mortality over 30 days using age, heart rate, and systolic blood pressure (SBP)[8]. Modified age, creatinine clearance, and ejection fraction score (mACEF) are calculated in patients undergoing percutaneous coronary intervention[9]. Some investigators have already tested these risk scores for long-term follow-up. The comparison among some risks scores have been done by several study groups[10-12]. Although some investigators have tested these risk scores to predict long-term mortality in patients with STEMI, there is still lack of evidence on their usefulness and in long-term follow-up, and moreover, we still do not have enough information about the superiority of these scores to each other. Therefore, herewith we tried to compare five different risk scores regarding to their predictive value for long-term all-cause mortality in patients with STEMI underwent PCI.

PATIENTS and METHODS

Study Design and Patients Selection

One thousand seven hundred and eighty (1780) patients had been admitted to our centre with STEMI and had undergone PCI between 2009-2013. Patients whose age was over 80 years (n= 55), patients with known or recently diagnosed cancer (n= 22); patients with inflammatory or connective-tissue disease (n= 10); and patients who died during PCI (n= 4) were excluded. Overall, 1689 patients were retrospectively enrolled to the study (Figure 1). The patients were followed up to 365 days. Medical data was obtained from electronic health records of the hospital. Each patient's mortality risk was assessed with five different risk scores and recorded. Risk scores were compared to each other. The study protocol complied with the Declaration of Helsinki.

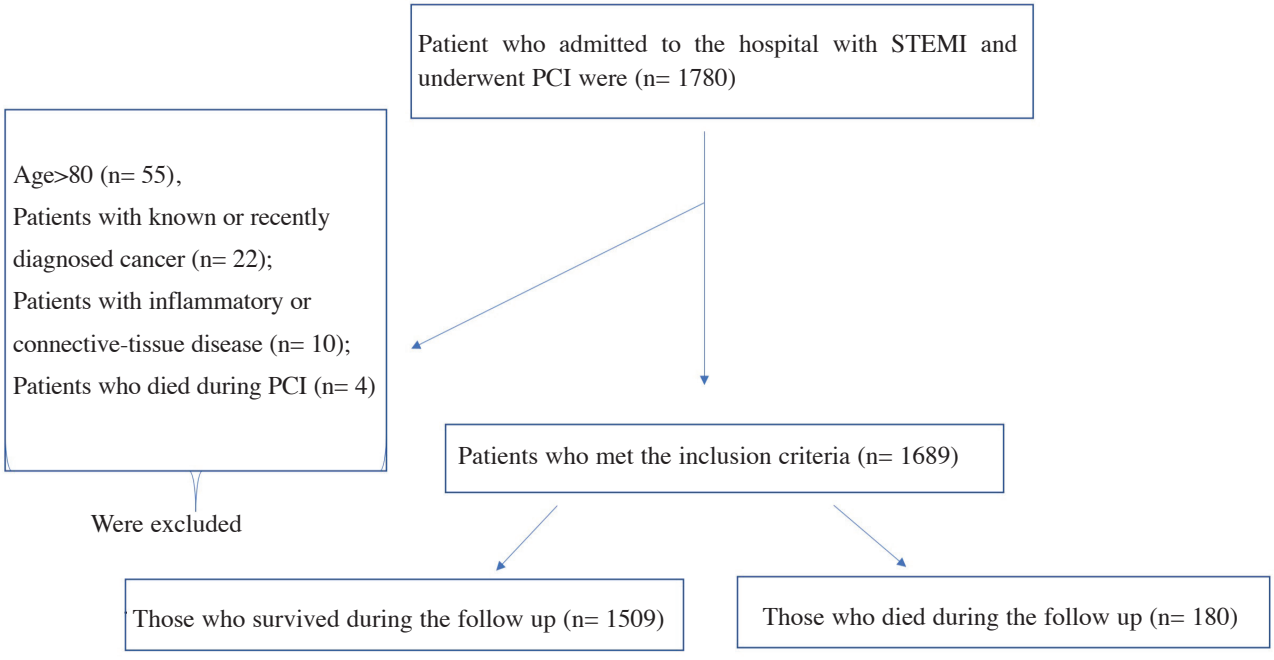

Figure 1. Study flow chart.

Definitions

STEMI was defined as typical chest pain accompanied by persistent ST-elevation at least two contiguous derivations or a new onset left bundle branch block (LBBB)[13].

Blood tests were obtained in all patients on admission or in the first 24 hours. Heart failure was assessed according to Killip classification[14]. A transthoracic echocardiography was performed by a Vivid 3 instrument (GE; Horten, Norway). Left ventricular ejection fraction (LVEF) was measured using modified Simpson method. Coronary angiographies were performed by Siemens Artis interventional angiography system[15]. Anaemia was haemoglobin (Hb) levels 12.0 g/dL in females and 13.0 g/dL in males[16]. The Cockcroft-Gault formula was used for estimating creatinine clearance in all patients[17]. All patients were treated according to relevant guidelines[18]. TIMI, PAMI CADILLAC, TIMI risk index, mACEF scores were calculated in all patients. Age, presence of diabetes mellitus (DM) or hypertension (HT) or anginal complaints, systolic blood pressure (SBP), heart rate, Killip class, weight, anterior myocardial infarction (MI)/new onset LBBB and ischemic time were used to calculate the TIMI score[3,5]. Age, Killip class, heart rate, presence of DM, anterior MI/new onset LBBB were used to calculate PAMI risk score[6]. CADILLAC risk score was calculated using LVEF, Killip class, renal failure, post TIMI flow, age, presence of anaemia and presence of three vessel disease. For relevant risk score, numerical points were assigned to each risk factor and therefore, the risk was calculated[7]. TRI was calculated using the following formula: [HR x $(age/10)^2$]/SBP. mACEF was calculated using the following formula: age/LVEF (%) + 1 point (for every 10 mL/min reduction in creatinine clearance below 60 mL/min/1.73 m^2) (up to a maximum of six points)[8,9].

Statistics

Percent and n were used for categorical variables. Median and interquartile range were used for numerical variables. The primary outcome was time to all-cause mortality. Mann-Whitney U test was used to compare continuous variables, and the χ^2 test or Fisher's exact test was used for categorical variables. All statistical analysis was carried out using R-software v. 3.5.1 (R statistical software, Institute for Statistics and Mathematics, Vienna, Austria). A p value of <0.05 was considered statistically significant.

RESULTS

Among these patients, 821 of them presented with anterior MI, 831 with inferior MI and 37 of them with posterior MI. Median age of the patients was 56 (IQR= 48-65). Overall, 80% of the patients were males. About 40% of the patients had HT, 22.7% had DM. More than half (55.1%) of the patients were smokers. Overall, 4.6% (n= 79) of the patients had cardiogenic shock. Clinical follow-up after PCI performed for a median of 365 days (IQR= 361-365). The number who died of all-cause mortality was 180. Patients' basal characteristics are presented in Table 1. Apart from high density lipoprotein (HDL) and platelet level, all laboratory and clinical values were statistically significantly different between the two groups who died of all-cause death and survived during the follow-up period. Those who died had a mean follow-up of 39.5 days (IQR= 3-192). According to multivariable Cox regression analyses, the mACEF score was the strongest predictor for all-cause death in patients with STEMI. Among all of these risk scores, the mACEF score had the highest predictive accuracy with a c-index of 0.850 and a likelihood ratio-X^2 of 324. Likewise, among all other risk scores, mACEF score was the best model to explain the variance with an adjusted R^2 of 0.227 (Table 2). In multivariable cox regression analyses, hazard ratios (HR) of the risk scores are demonstrated in Table 3. The CADILLAC risk score has the highest HR with a value of 13.0 (95% CI, 6.29-26.8) among the other risk scores, yet the confidence interval is quite wide. On the contrary, TRI had the lowest HR with a value of 2.32 (95% CI, 1.36-3.66). Both risk models have the same statistical significance in predicting one-year all-cause mortality (Table 3). Adjusted hazard ratio plots for relevant scoring systems are presented in Figure 2. Besides, AUCROC comparison of the models are presented in Figure 3.

DISCUSSION

Among five scores, the mACEF score was demonstrated to be the strongest model in terms of predicting one-year all-cause death. Although the other four scores were demonstrated to have similar statistically significant predictive value, the performance of the relevant risk scores may alter in clinical respect.

Despite the advances in medical and invasive therapy, coronary artery disease remains to be the most common cause of death worldwide[19].

Specifically, mortality rates differ in patients with STEMI in different trials, which indicates the importance of risk stratification and maintenance therapy after appropriate invasive procedure[20].

Previously, several studies have demonstrated the strength of different risk scores in different patient cohorts, yet each score had its own disadvantages especially in terms of application in clinical practice[21-24]. Among these disadvantages, the time of obtaining required data such as angiographic futures, observer dependency interpreting for categoric variables, the duration of concomitant disease involved in the scoring systems such as DM can be counted among these disadvantages.

Table 1. Comparison of baseline characteristics between the survivors and dead patients

Variables	All patients n= 1689	All cause death (-) n= 1509	All cause death (+) n= 180	p
Age	56 (48-65)	55 (47-63)	69 (57-76)	<0.001
Sex (male) (n %)	1359	1237	122	<0.001
HT (n %)	682 (40.4%)	584	98	<0.001
DM (n %)	384 (22.7%)	298	79	<0.001
Smoke (n %)	930 (55.1%)	860	70	<0.001
MI-pattern (n %)				0.005
1	821 (48.6%)	713	108	
2	831 (49.2%)	763	68	
3	37 (2.2%)	33	4	
Total ischemic time (minutes)	172 (110-258)	163 (105-240)	236 (152-338)	<0.001
Troponin	3.2 (1.2-12)	1.78 (0.65-4.23)	3.45 (1.42-10.9)	<0.001
LDL	110 (84-138)	111 (85-140)	102 (75.8-125)	0.007
HDL	37 (31-45)	38 (31.4-45)	35 (28.5-45.8)	0.566
Triglyceride	119 (84-167)	120 (84-170)	114 (87-159)	0.079
Total cholesterol	175 (148-202)	176 (150-205)	165 (135-194)	0.002
BNP	69 (36-132)	62 (34-104)	224 (91-434)	<0.001
CRP	9.8 (5.6-16.7)	9.10(5.3-15.4)	21.1 (12.3-34.2)	<0.001
LVEF	48 (42-55)	50 (45-55)	38 (32-45)	<0.001
GFR	88 (72-104)	90 (75-105)	63 (44-82)	<0.001
HB	13.9 (12.8-15)	14.0 (13.0-15.0)	13.2 (11.2-14.3)	<0.001
WCB	11.8 (9.65-14.2)	11.6 (9.60-14.0)	13.6 (10.2-17.4)	<0.001
PLT	250 (213-298)	248 (212-297)	259 (214-302)	0.294
Creatinine	0.87 (0.72-1.0)	0.85 (0.75-0.99)	1.04 (0.90-1.50)	<0.001
TIMI	2 (1-4)	2 (1-4)	5 (3.75-7)	<0.001
TRI	17.7 (12.6-25.1)	17.1 (12.3-23.8)	26.7 (16.9-40.4)	<0.001
PAMI	2 (0-5)	2 (0-4)	6 (3-9)	<0.001
CADILLAC	2 (0-4)	2 (0-4)	8 (5-11)	<0.001
mACEF	1.19 (0.96-1.53)	1.14 (0.94-1.41)	2.14 (1.58-4.00)	<0.001
Shock	79 (4.6%)	29 (1.9%)	50 (%27)	<0.001

HT: Hypertension, DM: Diabetes mellitus, MI: Myocardial infarction, LDL: Low density lipoprotein, HDL: High density lipoprotein, BNP: Brain natriuretic peptide, CRP: C-reactive protein, LVEF: Left ventricle ejection fraction, GFR: Glomerular filtration rate, HB: Haemoglobin, WBC: White blood cell, PLT: Platelet, TIMI: Thrombolysis in myocardial infarction, TRI: TIMI risk index, PAMI: The primary angioplasty in myocardial infarction, CADILLAC: The controlled abciximab and device investigation to lower late angioplasty complications, mACEF: Modified age, creatinine clearance, and ejection fraction score.

Table 2. Multivariable cox regression analyses for different risk scoring systems

Scores	Likelihood ratio-X^2	R^2	c-index (AUC)	AIC	BIC
TRI	148	0.107	0.704	2495	2517
PAMI	235	0.165	0.796	2408	2430
TIMI	190	0.135	0.771	2452	2468
CADILLAC	319	0.223	0.844	2280	2296
mACEF	324	0.227	0.850	2277	2298

TRI: TIMI risk index, PAMI: The primary angioplasty in myocardial infarction, TIMI: Thrombolysis in myocardial infarction, CADILLAC: The controlled abciximab and device investigation to lower late angioplasty complications, mACEF: Modified age, creatinine clearance, and ejection fraction score, AIC: Akaike information criterion, BIC: Bayesian information criterion.

Table 3. Multivariable Cox proportional regression for all-cause-death

Scores	Hazard ratio, 95% CI	p
TRI (change from 12.6 to 25.1)	2.32 (1.36-3.66)	<0.001
TIMI (change from 1 to 4)	5.22 (2.85-9.57)	<0.001
PAMI (change from 0 to 5)	6.95 (3.77-12.8)	<0.001
CADILLAC (change from 0 to 5)	13.0 (6.29-26.8)	<0.001
mACEF (change from 0.96 to 1.53)	9.13 (4.02-20.7)	<0.001

TRI: TIMI risk index, PAMI: Primary angioplasty in myocardial infarction, TIMI: Thrombolysis in myocardial infarction, CADILLAC: The controlled abciximab and device investigation to lower late angioplasty complications, mACEF: Modified age, creatinine clearance, and ejection fraction score.

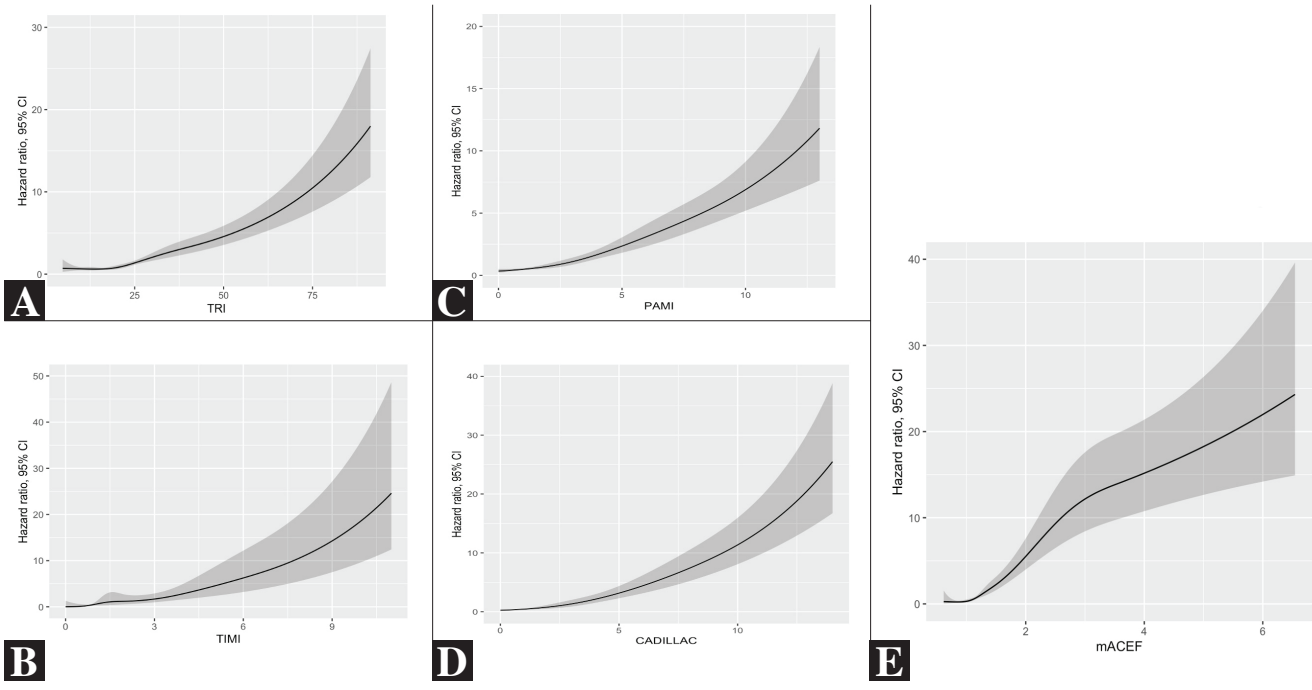

Figure 2. Adjusted hazard ratio plot.

In order to provide both accurate and practical evaluation, risk assessment should be based on objective parameters rather than subjective parameters. Another issue is the cohort that we work on. For example, while TIMI and GRACE score demonstrated to have similar predictive performance in STEMI patients, the GRACE score was demonstrated to be better in clinical practice in terms of its applicability to all spectrum of acute coronary syndromes[25].

Another study comparing two risk scores (TIMI and CADILLAC) in terms of predicting in-hospital mortality in patients presented with STEMI and without cardiogenic shock, similar statistical significance has been demonstrated. Despite the similarity in statistical significance between the two scores, the TIMI risk score was superior to CADILLAC score according to c-index[26]. In our study, CADILLAC score demonstrated to be better than TIMI with a c-index of 0.844 vs 0.771, respectively (Table 2).

This difference might be attributed to the longer follow-up period and a more heterogeneous patient population.

In another study by Huang et al., mACEF has been found superior to ACEF and GRACE score predicting in-hospital death in STEMI patients, yet there was no significant difference in NSTEMI patients[27].

According to the study of Kao et al. comparing the TIMI, GRACE, PAMI and CADILLAC risk scores in Taiwanese diabetic patients with STEMI, they have not included mACEF score to their study and demonstrated that CADILLAC risk score is the most effective model predicting six months, one year and two years all-cause mortality. In another study carried out by Lev et al., TIMI, PAMI, GRACE and CADILLAC score

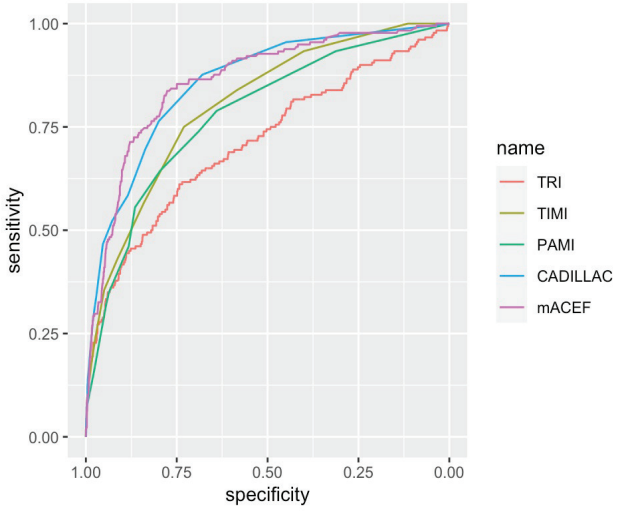

Figure 3. AUCROC comparison of the models.

have been compared. According to c-statistics, TIMI and PAMI scores performed similar and well yet, CADILLAC score achieved the best performance in terms of predicting 30-days and one year mortality. The strength of CADILLAC scoring system was attributed to its ability to give information about angiographic features, LVEF and presence of anaemia, which are already indicators for poor prognosis[28,29].

In our study, CADILLAC score was demonstrated to be the strongest model after mACEF score. Although mACEF score is calculated using a few parameters comparing with relevant scores, it is still demonstrated to be the strongest to predict long-term all cause-death in clinical respect. The less component a model includes, the more applicable it is for clinical practice. CADILLAC score could be interpreted only after coronary angiography, on the other hand, mACEF score could be calculated on admission, and our results confirm its reliability in predicting long-term all-cause mortality in STEMI patients. Another problem we may encounter in scoring systems with multiple parameters is that they are not user friendly and practical. We tried to compare the models including variables easier to obtain at admission and during the intervention procedure. Some parameters including relevant scoring systems are relatively subjective such as Killip score. On the other hand, creatinine clearance and age are not debatable values depending on observers and are already determinants of poor prognosis. Therefore, better predictive value of the mACEF risk score among other scoring models may be attributed to the more objective components of the model. Ejection fraction, which is included in mACEF, is already a well-known determinant for long-term survival in patients with STEMI[28].

Limitations

The main limitation of our study is the retrospective nature of the study design. Secondly, the follow-up period is relatively short comparing with similar studies. Thirdly, the duration of DM, and if present, chronic kidney disease were not known, therefore the effect of the relevant disease on cardiovascular system cannot be interpreted very clearly for each person. Another limitation is, considering the wide ranges of confidence intervals, the study population was small in numbers, therefore further investigations should be carried out for more certain results.

Finally, a large scale prospective, multicentre study is required for comparing the risk scores and to decide on both the simplest and the strongest model to apply to our clinical practice.

CONCLUSION

Although similar statistical significance was presented among all scores, mACEF was demonstrated to be the strongest model among all five risk scores to predict long-term all-cause mortality in clinical respect.

Ethics Committee Approval: The study was approved by the ethics committee of Kartal Koşuyolu High Specialization Training and Research Hospital Clinical Research Ethics Committee (Decision no: 2022/13/626, Date: 06.09.2022).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - FÖK; Analysis/Interpretation - İHT, AK; Data Collection - TÖ, MS; Writing - VO; Critical Revision - AK; Statistical Analysis - İHT; Overall Responsibility - FÖK.

Conflict of Interest: The authors have no conflicts of interest to declare.

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

REFERENCES

1. Schiele F, Hochadel M, Tubaro M, Meneveau N, Wojakowski W, Gierlotka M, et al. Reperfusion strategy in Europe: Temporal trends in performance measures for reperfusion therapy in ST-elevation myocardial infarction. Eur Heart J 2010;31(21):2614-24. [Crossref]
2. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2018;39(2):79-82. [Crossref]
3. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, Lemos JA de, et al. TIMI risk score for ST-elevation myocardial infarction: A convenient, bedside, clinical score for risk assessment at presentation an intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation 2000;102:2031-7. [Crossref]

4. Kozieradzka A, Kamiński KA, Maciorkowska D, Olszewska M, Dobrzycki S, Nowak K, et al. GRACE, TIMI, Zwolle and CADILLAC risk scores-do they predict 5-year outcomes after ST-elevation myocardial infarction treated invasively? Int J Cardiol 2011;148:70-5. [Crossref]
5. Morrow DA, Antman EM, Parsons L, de Lemos JA, Cannon CP, Giugliano RP, et al. Application of the TIMI risk score for ST-elevation MI in the National Registry of Myocardial Infarction 3. JAMA 2001;286:1356-9. [Crossref]
6. Addala S, Grines CL, Dixon SR, Stone GW, Boura JA, Ochoa AB, et al. Predicting mortality in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score). Am J Cardiol 2004;93:629-32. [Crossref]
7. Halkin A, Singh M, Nikolsky E, Grines CL, Tcheng JE, Garcia E, et al. Prediction of mortality after primary percutaneous coronary intervention for acute myocardial infarction. The CADILLAC risk score. J Am Coll Cardiol 2005;45:1397-405. [Crossref]
8. Morrow DA, Antman EM, Giugliano RP, Cairns R, Charlesworth A, Murphy SA, et al. A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction: An InTIME II sub-study. Lancet 2001;358(9293):1571-5. [Crossref]
9. Wykrzykowska JJ, Garg S, Onuma Y, de Vries T, Goedhart D, Morel MA, et al. Value of age, creatinine, and ejection fraction (ACEF score) in assessing risk in patients undergoing percutaneous coronary interventions in the 'All-Comers' LEADERS trial. Circ Cardiovasc Interv 2011;4:47-56. [Crossref]
10. Littnerova S, Kala P, Jarkovsky J, Kubkova L, Prymusova K, Kubena P, et al. GRACE score among six risk scoring systems (CADILLAC, PAMI, TIMI, Dynamic TIMI, Zwolle) demonstrated the best predictive value for prediction of long-term mortality in patients with ST-elevation myocardial infarction. PLoS One 2015;10(4):e0123215. [Crossref]
11. Kao YT, Hsieh YC, Hsu CY, Huang CY, Hsieh MH, Lin YK, et al. Comparison of the TIMI, GRACE, PAMI and CADILLAC risk scores for prediction of long-term cardiovascular outcomes in Taiwanese diabetic patients with ST-segment elevation myocardial infarction: From the registry of the Taiwan Society of Cardiology. PLoS One 2020;15(2):e0229186. [Crossref]
12. Lev EI, Kornowski R, Vaknin-Assa H, Porter A, Teplitsky I, Ben-Dor I, et al. Comparison of the predictive value of four different risk scores for outcomes of patients with ST-elevation acute myocardial infarction undergoing primary percutaneous coronary intervention. Am J Cardiol 2008;102:6-11. [Crossref]
13. Thygesen K, Alpert JS, White HD. Task force members, ESC Committee for practice guidelines, document reviewers, universal definition of myocardial infarction: Kristian Thygesen, Joseph S. Alpert and Harvey D. White on behalf of the Joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. Eur Heart J 2007;28(20):2525-38. [Crossref]
14. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. Am J Cardiol 1967;20(4):457-64. [Crossref]
15. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification. Eur J Echocardiogr 2006;7(2):79-108. [Crossref]
16. Blanc B, Finch CA, Hallberg L, Herbert V, Lawkowicz W, Layrisse M. Nutritional anaemias. Report of a WHO Scientific Group. WHO Tech Rep Ser 1968:1-40.
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16(1):31-41. [Crossref]
18. Van de Werf F, Ardissino D, Betrui A, Cokkinos DV, Falk E, Fox KA, et al. Management of acute myocardial infarction in patients with ST-segment elevation. Eur Heart J 2003;24:28-66. [Crossref]
19. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. Task force on the management of ST-elevation acute myocardial infarction of the European Society of Cardiology (ESC). ESC guidelines for management of acute myocardial infarction in patientspresenting with ST-segment elevation. Eur Heart J 2012;33:2569-619. [Crossref]
20. Windecker S, Hernández-Antolín RA, Stefanini GG, Wijns W, Zamorano JL. Management of ST-elevation myocardial infarction according to European and American guidelines. EuroIntervention 2014;10:23-31. [Crossref]
21. Schellings DA, Adiyaman A, Giannitsis E, Hamm C, Suryapranata H, Ten Berg JM, et al. Early discharge after primary percutaneous coronary intervention: The added value of N-terminal pro-brain natriuretic peptide to the Zwolle Risk Score. J Am Heart Assoc 2014;3:e001089. [Crossref]
22. Raposeiras-Roubín S, Abu-Assi E, Cabanas-Grandío P, Agra-Bermejo RM, Gestal-Romarí S, Pereira-López E, et al. Walking beyond the GRACE (Global Registry of Acute Coronary Events) model in the death risk stratification during hospitalization in patients with acute coronary syndrome: What do the AR-G [ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry and GWTG (Get With the Guidelines) Database], NCDR (National Cardiovascular Data Registry), and EuroHeart Risk Scores Provide? JACC Cardiovasc Interv 2012;5:1117-25. [Crossref]
23. Brkovic V, Dobric M, Beleslin B, Giga V, Vukcevic V, Stojkovic S, et al. Additive prognostic value of the SYNTAX score over GRACE, TIMI, ZWOLLE, CADILLAC and PAMI risk scores in patients with acute ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention. Int J Cardiovasc Imaging 2013;29:1215-28. [Crossref]
24. Méndez-Eirín E, Flores-Ríos X, García-López F, Pérez-Pérez AJ, Estévez-Loureiro R, Piñón-Esteban P, et al. Comparison of the prognostic predictive value of the TIMI, PAMI, CADILLAC, and GRACE risk scores in STEACS undergoing primary or rescue PCI. Rev Esp Cardiol 2012;65:227-33. [Crossref]
25. Chan Pin Yin D, Azzahhafi J, James S. Risk assessment using risk scores in patients with acute coronary syndrome. J Clin Med 2020;9(9):3039. [Crossref]
26. González-Pacheco H, Arias-Mendoza A, Álvarez-Sangabriel A, Juárez-Herrera Ú, Damas F, Eid-Lidt G, et al. The TIMI risk score for STEMI predicts in-hospital mortality and adverse events in patients without cardiogenic shock undergoing primary angioplasty. Arch Cardiol Mex 2012;82(1):7-13.
27. Huang J, Wei X, Wang Y, Jiang M, Lin Y, Su Z, et al. Comparison of prognostic value among 4 risk scores in patients with acute coronary syndrome: Findings from the improving care for cardiovascular disease in China-ACS (CCC-ACS) Project. Med Sci Monit 2021;27:e928863. [Crossref]
28. Halkin A, Stone GW, Dixon SR. Impact, and determinants of left ventricular function in patients undergoing primary percutaneous coronary intervention in acute myocardial infarction. Am J Cardiol 2005;96:325-31. [Crossref]
29. Nikolsky E, Aymong ED, Halkin A, Grines CL, Cox DA, Garcia E, et al. Impact of anemia in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: Analysis from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial. J Am Coll Cardiol 2004;44:547-53. [Crossref]

Atrial Dispersion Predicts Atrial Fibrillation in Mitral Stenosis: A Five-Year Follow-Up Speckle-Tracking Echocardiography Study

Özkan Candan(İD)

Department of Cardiology, Uşak University Faculty of Medicine, Uşak, Türkiye

ABSTRACT

Introduction: Atrial dispersion showing increased electrical heterogeneity may be associated with the occurence of atrial fibrillation (AF). In our study, it was aimed to investigate the effects of atrial dispersion evaluated by speckle tracking echocardiography on the occurence of AF on in patients with mild to moderate rheumatic mitral stenosis.

Patients and Methods: Sixty-two patients with rheumatic mitral stenosis with sinus rhythm, asymptomatic or NYHA 1 symptoms were included in the study. The time to peak atrial strain was measured for each segment by speckle tracking echocardiography in two and four-chamber views. Atrial dispersion was calculated by taking the standard deviation of time to peak strain in 12 left atrial segments. Echocardiographic and clinical parameters of the patients were compared according to the development of AF.

Results: During follow-up (mean follow-up duration, 49.9 ± 12.9 months), 19 patients (30%) developed AF. Compared to patients who did not develop AF at follow-up, patients with AF were older (46.8 ± 10.2 vs. 35.9 ± 12, p= 0.001), while mitral valve area (MVA) (1.38 ± 0.1 vs. ± 1.49 ± 0.18 vs. p= 0.02), PALS (13.7 ± 4 vs. 18.8 ± 5.5, p= 0.001) and PACS (6 ± 2.3 vs. 8.2 ± 3.8, p= 0.002) were found to be lower. Atrial dispersion was found to be increased in patients who developed AF (63.2 ± 13.5 vs. 46.1 ± 22.3, p= 0.003). Age, atrial dispersion and PALS were determined as independent predictors of AF development in Cox regression analysis.

Conclusion: Atrial dispersion, a new parameter measured by STE, predicts the development of AF. Increased atrial dispersion may provide additional benefits in initiating prophylactic antiarrhythmic drug therapy or anticoagulants.

Key Words: Mitral valve stenosis; atrial fibrillation; 2D echocardiography

Mitral Darlığı Hastalarında Atriyal Dispersiyon Atriyal Fibrilasyon Gelişmesini Öngördürür: Beş Yıllık Noktacık Takipli Ekokardiyografi Çalışması

ÖZET

Giriş: Artmış elektriksel heterojeniteyi gösteren atriyal dispersiyon, atriyal fibrilasyon (AF) gelişimi ile ilişkili olabilir. Çalışmamızda hafif ve orta dereceli romatizmal mitral darlığı olan hastalarda noktacık takipli ekokardiyografi ile değerlendirilen atriyal dispersiyonun AF üzerindeki etkilerini araştırdık.

Hastalar ve Yöntem: Çalışmaya sinüs ritminde, asemptomatik veya NYHA 1 semptomları ve romatizmal mitral darlığı olan 62 hasta alındı. Zirve atriyal gerilime kadar geçen süre, iki ve dört odacıklı görüntülerde noktacık takipli ekokardiyografi ile her segment için ölçüldü. Atriyal dispersiyon, tüm 12 sol atriyal segmentte zirve gerilime kadar geçen zamanın standart sapması alınarak ölçüldü. Takip süresinde hastaların ekokardiyografik ve klinik parametreleri AF gelişimine göre karşılaştırıldı.

Bulgular: Takip süresi boyunca (ortalama takip süresi 49.9 ± 12.9 ay), 19 hastada (%30) AF gelişti. Takipte AF gelişmeyen hastalar ile karşılaştırıldığında, AF gelişen hastaların yaşı daha fazla iken (46.8 ± 10.2'ye karşı 35.9 ± 12, p= 0.001), mitral kapak alanı (MVA) (1.38 ± 0.1'e karşı 1.49 ± 0.18, p= 0.02), PALS (13.7 ± 4'e karşı 18.8 ± 5.5, p= 0.001) ve PACS (6 ± 2.3'e karşı 8.2 ± 3.8, p= 0.002), daha düşük saptandı. Ancak atriyal dispersiyon (63.2 ± 13.5'e karşılık 46.1 ± 22.3, p= 0.003) AF'si olan hastalarda artmış olarak saptandı. Çok değişkenli Cox regresyon analizinde yaş, atriyal dispersiyon ve PALS, takipte AF gelişimi için bağımsız öngörücü olarak tespit edildi.

Sonuç: Noktacık takipli ekokardiyografi ile değerlendirilen atriyal dispersiyon, AF gelişimi ile ilişkilidir. Atriyal dispersiyon, antiaritmik ilaç tedavisinin veya antikoagülan tedavinin erken başlatılması için ek bilgi sağlayabilir.

Anahtar Kelimeler: Mitral kapak darlığı; atriyal fibrilasyon; 2D ekokardiyografi

Cite this article as: *Candan Ö. Atrial dispersion predicts atrial fibrillation in mitral stenosis: A five-year follow-up speckle-tracking echocardiography study Koşuyolu Heart J 2023;26(1):27-33.*

Correspondence

Özkan Candan

E-mail: oz_candan@hotmail.com
Submitted: 27.10.2022
Accepted: 25.01.2023
Available Online Date: 21.03.2023

INTRODUCTION

Rheumatic heart disease affects the mitral valves and causes mitral stenosis very frequently. Despite advances, morbidity causes such as peripheral and cerebral embolic events, pulmonary edema, and deterioration in quality of life are still high[1,2]. The frequency of atrial fibrillation (AF) in mitral stenosis has been found to be 30-50%[3]. In mitral stenosis, increased atrial pressure causes inflammation and interstitial fibrosis in the atrial wall, leading to a decrease in atrial wall elasticity. The structural remodeling process leads to electrical remodeling and causes AF[4]. Many clinical, echocardiographic and biochemical variables that cause AF in patients with mitral stenosis have been investigated[5-7]. Two-dimensional (2D) strain imaging as assessed by speckle tracking echocardiography (STE) has been developed to examine both ventricular and atrial myocardial function[8-11].

Atrial dispersion with electrical heterogeneity has been found to be associated with occurence of AF in the normal population[12-14]. In patients with reduced atrial dispersion, recurrence of AF was reduced after successful ablation[15].

In this study, it was aimed to investigate whether atrial strain and atrial dispersion used together with clinical parameters are associated with occurence of AF.

PATIENTS and METHODS

One hundred and twenty patients with mild or moderate rheumatic mitral stenosis were screened. Inclusion criteria were determined as patients with mild or moderate rheumatic mitral stenosis, asymptomatic patients and patients with EF> 65%, and 82 patients meeting the inclusion criteria were included in the study.

Exlucia criteria was described as anemia, chronic obstrictive pulmonary disease, hypertension, history of coronary artery intervention, NYHA class II-IV, modorate or severe aortic or mitral or tricuspid insufficiency. Eleven patients who did not come to the follow-up appointment and nine patients with inapropiate echocardiographic images were excluded from the study.

A 12-lead ECG was taken at each examination, and cardiac symptoms were evaluated. A rhythm Holter recording was done when the patient had symptoms suggestive of AF. AF was determined as rhythm without p waves and irregular RR intervals in 12 lead ECG[16].

Classic 2D-Echocardiography

All echocardiographic images were gathered by a Vivid 7 machine using a 3.5 MHz transducer. The acquired images were analyzed offline with the EchoPAC program. Data of classic 2D echocardiography and dopplers measurements were collected in accordance with the guidelines[17-20].

Speckle Tracking Echocardiography

Apical 2 and 4 chambers view has been used to evaluate left atrail strain. The narrowest volume of left atrial endocardium was marked manually. Additional lines were created automatically in the epicardial and middle myocardial regions with the software. Before the analysis, it was checked whether the line formed was visually appropriate for endocardial follow-up. If not appropriate, it was corrected again manually. Left atrial endocardium was divided into six segments.

Peak atrial longitudinal stretch (PALS) was defined as the strain in the left atrium reaching its largest volume while (PACS) was defined as the strain immediately after the p wave in the ECG. In total, strain analysis was performed on 744 segments, and 3.9% of the segments were not included in the study.

Time from the onset of the QRS complex to the peak strain was calculated for each left atrial wall segment. Standard deviation of the electrical delay of a total of 12 segments was calculated and defined as the atrial dispersion[14].

Our study adhered to the Helsinki Declaration, and all patients provided written informed consent. The Ethics Committee of Kartal Koşuyolu High Specialization Training and Research Hospital approved the study in İstanbul, Türkiye.

Statistical Analysis

In the analysis of continuous variables between the two groups, Student's t test or Mann-Whitney U test was used, depending on whether it showed normal distribution or not. $\chi 2$ or Fisher's exact test was used for categorical variables, and Pearson's correlation test was used for correlation analysis. Cox regression testing was used to identify predictors contributing to the development of AF. Variables that were significant in a single analysis were used to perform multivariate analysis. For statistical significance, p value was determined as <0.05 and SPSS (version 24.0) program was used.

RESULTS

Sixty-two patients with isolated mild-to-moderate mitral stenosis (40% male, mean age 39.2 ± 12.5 years) were included in the study. Clinical features and echocardiographic data of the study patients are shown in Table 1.

Atrial fibrillation was detected in 19 patients (30%) during the follow-up period (mean follow-up= 49.9 ± 12.9 months). Eight of these patients had paroxysmal and 11 had persistent AF.

Table 1. Echocardiographic and clinical characteristic of the study population

Variable	All patients n= 62	AF (+) n= 19	AF (-) n= 43	p
Age (years)	39.2 ± 12.5	46.8 ± 10.2	35.9 ± 12	0.001
Sex (male) (%)	25 (40%)	5 (26%)	20 (47%)	0.1
Body surface area (m^2)	1.69 ± 0.13	1.67 ± 0.12	1.7 ± 0.14	0.5
Systolic blood pressure (mmHg)	128.9 ± 8.1	129.3 ± 7.5	128.7 ± 8.4	0.7
Diastolic blood pressure (mmHg)	78.4 ± 5.7	79.8 ± 6.6	77.7 ± 5.3	0.1
Heart rate (bpm)	72.6 ± 9.1	75 ± 8.3	71.6 ± 9.4	0.1
LVEF (%)	63.8 ± 4.1	64.7 ± 4	63.3 ± 4.2	0.2
LA diameter (cm)	5 ± 0.5	5 ± 0.5	4.9 ± 0.5	0.7
LAVi (mL/m^2)	57.1 ± 15.5	62.1 ± 20.3	54.9 ± 12.4	0.1
E (m/s)	2.2 ± 0.5	2.2 ± 0.6	2.2 ± 0.6	0.8
A (m/s)	1.88 ± 0.47	1.7 ± 0.48	1.9 ± 0.47	0.2
PALS (%)	17.2 ± 5.6	13.7 ± 4	18.8 ± 5.5	<0.001
PACS (%)	7.5 ± 3.5	6 ± 2.3	8.2 ± 3.8	0.008
Pulmonary artery pressure	36.7 ± 5.7	37.1 ± 6.4	36.6 ± 5.5	0.7
Atrial dispersion (msn)	51.4 ± 21.4	63.2 ± 13.5	46.1 ± 22.3	0.001
MVA by planimetry (cm^2)	1.46 ± 0.18	1.38 ± 0.15	1.49 ± 0.18	0.025
MVA by PHT (cm^2)	1.47 ± 0.16	1.47 ± 0.16	1.46 ± 0.16	0.8
Maximum gradient (mmHg)	16.9 ± 4.8	17.3 ± 3.9	16.7 ± 5.1	0.6
Mean gradient (mmHg)	8.2 ± 3	8.4 ± 2.9	8.2 ± 3	0.7

LVEF: Left ventricular ejection fraction, LA: Left atrial, LAVi: Left atrial volume index, PALS: Peak atrial longitudinal strain, PACS: Peak atrial contraction strain, E: Peak early filling transmitral velocity, A: Peak late filling transmitral velocity, MVA: Mitral valve area, PHT: Pressure half time, PLN: Planimetric.

Patients who developed AF were older than those who did not (46.8 ± 10.2 vs. 35.9 ± 12, p= 0.001). MVA (PLN) (1.38 ± 0.15 vs. 1.49 ± 0.18, p= 0.025) and global PALS (%) (13.7 ± 4 vs. 18.8 ± 5.5, p≤ 0.001) and global PACS (%) (6 ± 2.3 vs. 8.2 ± 3.8, p= 0.008) were statistically significantly lower in patients who developed AF (Table 1) (Figure 1).

Atrial dispersion was found to be statistically significantly prolonged in patients with AF (63.2 ± 13.5 vs. 46.1 ± 22.3 p= 0.001) (Table 1) (Figures 2, 3). However, the relation between atrial dispersion and AF type (permanent or paroxysmal) could not be determined (60.8 ± 7.5 ms vs. 66.4 ± 19.2, p= 0.45). There was no significant difference between the two groups in terms of left atrial diameter, left atrial volume index, and pulmonary artery systolic pressure (Table 1).

No significant correlation was observed between atrial dispersion (ms) and age (years), left atrial diameter (cm), left atrial volume index (mL/m^2), PALS (%), PACS (%), MVA PHT, maximum gradient and mean gradient. Only a moderate correlation was observed between atrial dispersion and MVA measured by the planimetric method (r= -0.38, p= 0.002).

Multivariate regression analysis was used to identify predictors of the development of AF. Atrial dispersion, PALS, age, and MVA (PLN), which were significant in the univariate analysis, were included in regression analysis. Atrial dispersion (ms) (HR= 1.033, 95 CI= 1.009-1.059, p= 0.008), age (years) (HR= 1.045, 95% CI= 1.001-1.091, p= 0.047) and PALS (HR= 0.868, 95%) (CI= 0.783-0.963, p= 0.007) were identified as independent predictors for the development of AF (Table 3).

DISCUSSION

Decreased PALS and greater atrial dispersion are associated with the occurence of AF in mitral stenosis.

Pressure increase in mitral stenosis causes an increase in interstitial fibrosis and contributes to the deterioration of atrial relaxation. As a result, the reservoir functions of the left atrium are impaired. Thus, electrical remodeling including shortening of the atrial effective refractory period and increased refractory period distribution may lead to the development of AF[21,22].

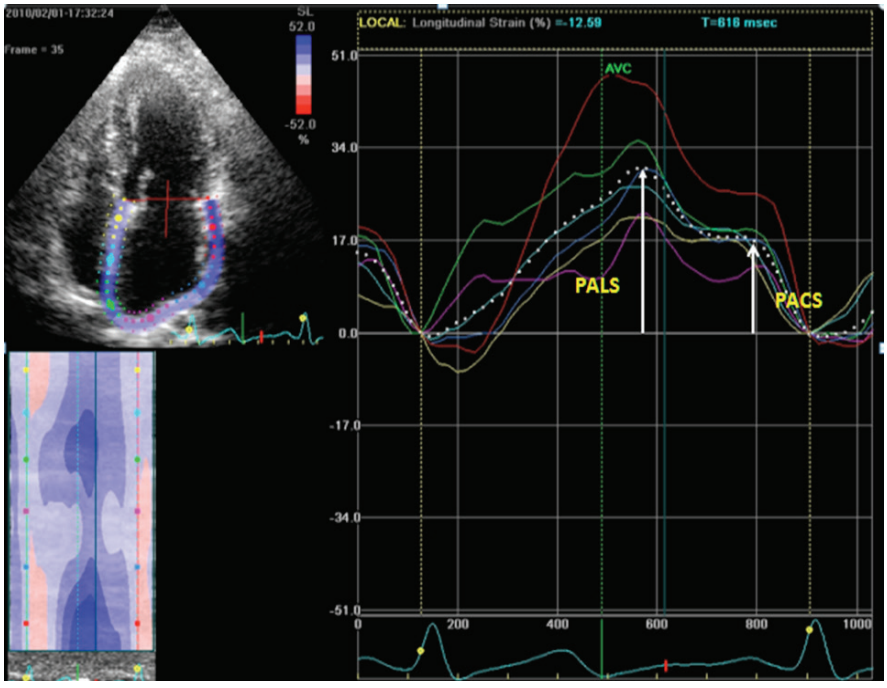

Figure 1. Left atrial longitudinal strain parameters.
PALS: Peak atrial longitudinal strain, PACS: Peak atrial contraction strain.

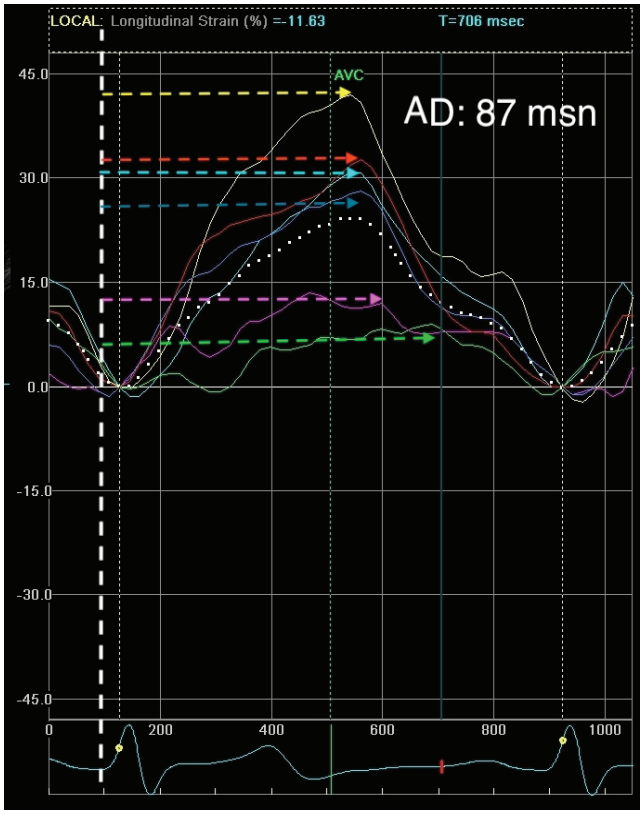

Figure 2. Speckle-based left atrial dispersion of with atrial fibrillation.
AD: Atrial dispersion.

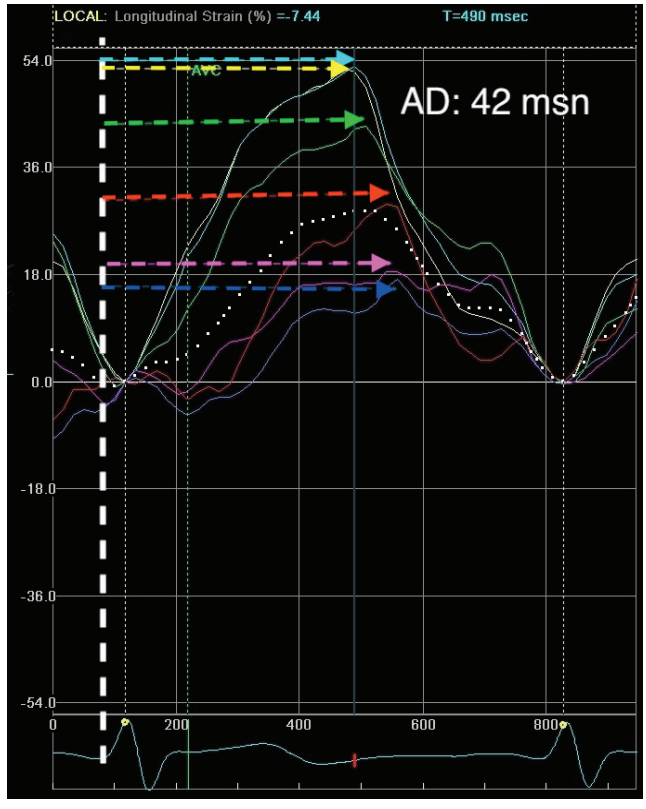

Figure 3. Speckle-based left atrial dispersion of without atrial fibrillation.
AD: Atrial dispersion.

Table 2. Correlation of atrial dispersion

Variable	r	p
Age (years)	0.52	0.6
PALS (%)	0.015	0.9
PACS (%)	0.006	0.9
LA diameter cm	-0.048	0.7
LAVi mL/m^2	-0.069	0.5
MVA (PLN)	-0.38	0.002
MVA (PHT)	0.091	0.4
Maximum gradient	0.022	0.8
Mean gradient	0.020	0.8

LA: Left atrial, LAVi: Left atrial volume index, PALS: Peak atrial longitudinal strain, PACS: Peak atrial contraction strain, MVA: Mitral valve area, PHT: Pressure half time, PLN: Planimetric.

Table 3. The results of cox regression analysis for the prediction of atrial fibrillation

Variable	B	Exp (B)	CI	p
Age (years)	0.044	1.045	1.001-1.091	0.047
PALS (%)	-0.141	0.868	0.783- 0.963	0.007
Atrial dispersion (msn)	0.033	1.033	1.009-1.059	0.008
MVA (PLN)	-1.031	0.357	0.023-5.654	0.46

PALS: Peak atrial longitudinal strain, CI: Confidence interval MVA: Mitral valve area, PLN: Planimetric.

PALS is used in the evaluation of reservoir function[9,10]. Decreased PALS may indicate impaired dilatation capacity (reservoir function) of the atrial tissue and may be useful in differentiating patients who may develop AF. PALS has been shown to be associated with the development of AF after cardiac surgery[23-25]. In addition to other echocardiographic and clinical parameters, LA strain has been found to be more accurate in predicting the development of AF in patients with mitral stenosis at follow up[26,27]. Similar to previous studies, in our study, global PALS was found to be predictive of the development of AF. Decreased PALS indicates impaired atrial reservoir function and thus, susceptibility to the development of AF.

Various diseases leading to fibrosis in the left ventricle and left atrium cause electrical asynchrony or dispersion by creating foci whose electrical stimulation occurs at different times. Subsequently, mechanical asynchrony may occur, triggering the formation of arrhythmia. Although atrial dispersion can be evaluated by various echocardiographic methods, it is more accurately and easily evaluated with speckle tracking echocardiography.

In a study of normal subjects predisposed to develop heart failure and AF, atrial dispersion has been found to be associated with the occurence of AF[28]. Atrial dispersion has been found to be associated with the occurence of recurrence in patients undergoing ablation for paroxysmal AF, and another study has found that prolonged atrial dispersion is significantly reduced after successful DC cardioversion in patients undergoing DC cardioversion in this patient group[15,29]. In a study by Kupczynska et al., increased atrial dispersion has been associated with the formation of thrombus in the atrial appendage[30]. In our study, atrial dispersion is associated with the development of AF. In patients with mitral stenosis, electrical heterogeneity in the atrial wall causes irregularities in conduction velocities and refractory periods. The resulting electrical remodeling can lead to electromechanical dysfunction and consequent development of AF[4]. According to the most recent ESC valvular diseases guideline, new onset AF contributes to the timing of decision for percutaneous mitral balloon valvuloplasty or surgical intervention in asymptomatic patients with mitral stenosis. Since atrial dispersion is also associated with AF in this patient group, it can be used to decide the time of intervention[31].

In this study, age was found to be associated with the occurence of AF. With increasing age, fibrosis in the atrial tissue increases more and leads to the development of AF[26].

CONCLUSION

Atrial dispersion as assessed by STE is associated with the development of AF. Atrial dispersion may provide additional information for the early initiation of antiarrhythmic drug therapy or anticoagulant therapy.

Limitations

The significant limitation is the study was that it was single-centered and the number of patients was relatively small. Since we did not have a special software for atrial strain assessment, the software used for ventricular strain assessment was utilized. Again, speckle tracking echocardiography evaluation was excluded from the analysis in some patients due to the requirement for good image quality. The frequency of AF may have been seen to be underestimated since the methods we used for detecting AF could not particularly detect patients with asymptomatic AF.

Ethics Committee Approval: This study was approved by Kartal Koşuyolu High Specialization Training and Research Clinical Research Ethics Committee (Decision no: 20/7/7/39, Date: 21.09.2017).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - ÖC; Analysis/Interpretation - ÖC; Data Collection - ÖC; Writing - ÖC; Critical Revision - AK; Final Approval - ÖC; Statistical Analysis - ÖC; Overall Responsibility - ÖC.

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

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

REFERENCES

1. Chandrashekhar Y, Westaby S, Narula J. Mitral stenosis. Lancet 2009;374(9697):1271-83. [Crossref]
2. Chugh SS, Blackshear JL, Shen WK, Hammill SC, Gersh BJ. Epidemiology and natural history of atrial fibrillation: Clinical implications. J Am Coll Cardiol 2001;37(2):371-8. [Crossref]
3. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. J Am Coll Cardiol 2021;77(4):450-500. [Crossref]
4. Josephson ME, Kastor JA, Morganroth J. Electrocardiographic left atrial enlargement. Electrophysiologic, echocardiographic and hemodynamic correlates. Am J Cardiol 1977;39(7):967-71. [Crossref]
5. Kim HJ, Cho GY, Kim YJ, Kim HK, Lee SP, Kim HL, et al. Development of atrial fibrillation in patients with rheumatic mitral valve disease in sinus rhythm. Int J Cardiovasc Imaging 2015;31(4):735-42. [Crossref]
6. Krishnamoorthy KM, Dash PK. Prediction of atrial fibrillation in patients with severe mitral stenosis-role of atrial contribution to ventricular filling. Scand Cardiovasc J 2003;37(6):344-8. [Crossref]
7. Ozaydin M, Turker Y, Varol E, Alaca S, Erdogan D, Yilmaz N, et al. Factors associated with the development of atrial fibrillation in patients with rheumatic mitral stenosis. Int J Cardiovasc Imaging 2010;26(5):547-52. [Crossref]
8. Karabay CY, Zehir R, Güler A, Oduncu V, Kalayci A, Aung SM, et al. Left atrial deformation parameters predict left atrial appendage function and thrombus in patients in sinus rhythm with suspected cardioembolic stroke: A speckle tracking and transesophageal echocardiography study. Echocardiography 2013;30(5):572-81. [Crossref]
9. Okamatsu K, Takeuchi M, Nakai H, Nishikage T, Salgo IS, Husson S, et al. Effects of aging on left atrial function assessed by two-dimensional speckle tracking echocardiography. J Am Soc Echocardiogr 2009;22(1):70-5. [Crossref]
10. Vianna-Pinton R, Moreno CA, Baxter CM, Lee KS, Tsang TSM, Appleton CP. Two-dimensional speckle-tracking echocardiography of the left atrium: Feasibility and regional contraction and relaxation differences in normal subjects. J Am Soc Echocardiogr 2009;22(3):299-305. [Crossref]
11. Saraiva RM, Demirkol S, Buakhamsri A, Greenberg N, Popović ZB, Thomas JD, et al. Left atrial strain measured by two-dimensional speckle tracking represents a new tool to evaluate left atrial function. J Am Soc Echocardiogr 2010;23(2):172-80. [Crossref]
12. Candan O, Gecmen C, Kahyaoğlu M, Şimsek Z, Çelik M, Uslu A, et al. Clinical utility of left atrial asynchrony and mechanical function in patients with hypertrophic cardiomyopathy. Acta Cardiol Sin 2022;38(2):141-50.
13. Shang Z, Su D, Cong T, Sun Y, Liu Y, Chen N, et al. Assessment of left atrial mechanical function and synchrony in paroxysmal atrial fibrillation with two-dimensional speckle tracking echocardiography. Echocardiography (Mount Kisco, NY). 2017;34(2):176-83. [Crossref]
14. Kawakami H, Ramkumar S, Nolan M, Wright L, Yang H, Negishi K, et al. Left atrial mechanical dispersion assessed by strain echocardiography as an independent predictor of new-onset atrial fibrillation: A case-control study. J Am Soc Echocardiogr 2019;32(10):1268-76.e3. [Crossref]
15. Sarvari SI, Haugaa KH, Stokke TM, Ansari HZ, Leren IS, Hegbom F, et al. Strain echocardiographic assessment of left atrial function predicts recurrence of atrial fibrillation. Eur Heart J Cardiovasc Imaging 2016;17(6):660-7. [Crossref]
16. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2021;42(5):373-498. [Crossref]
17. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. Eur J Echocardiogr 2009;10(1):1-25. [Crossref]
18. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015;16(3):233-70. [Crossref]
19. Schabelman S, Schiller NB, Silverman NH, Ports TA. Left atrial volume estimation by two-dimensional echocardiography. Cathet Cardiovasc Diagn 1981;7(2):165-78. [Crossref]
20. Pepi M, Tamborini G, Galli C, Barbier P, Doria E, Berti M, et al. A new formula for echo-Doppler estimation of right ventricular systolic pressure. J Am Soc Echocardiogr 1994;7(1):20-6. [Crossref]
21. Jaïs P, Peng JT, Shah DC, Garrigue S, Hocini M, Yamane T, et al. Left ventricular diastolic dysfunction in patients with so-called lone atrial fibrillation. J Cardiovasc Electrophysiol 2000;11(6):623-5. [Crossref]
22. Satoh T, Zipes DP. Unequal atrial stretch in dogs increases dispersion of refractoriness conducive to developing atrial fibrillation. J Cardiovasc Electrophysiol 1996;7(9):833-42. [Crossref]
23. Cameli M, Lisi M, Reccia R, Bennati E, Malandrino A, Solari M, et al. Pre-operative left atrial strain predicts post-operative atrial fibrillation in patients undergoing aortic valve replacement for aortic stenosis. Int J Cardiovasc Imaging 2014;30(2):279-86. [Crossref]
24. Pham TD, Fenoglio JJJ. Right atrial ultrastructural in chronic rheumatic heart disease. Int J Cardiol 1982;1(3-4):289-304. [Crossref]

25. Verdejo HE, Becerra E, Zalaquet R, Del Campo A, Garcia L, Troncoso R, et al. Atrial function assessed by speckle tracking echocardiography is a good predictor of postoperative atrial fibrillation in elderly patients. Echocardiography 2016;33(2):242-8. [Crossref]

26. Pourafkari L, Ghaffari S, Bancroft GR, Tajlil A, Nader ND. Factors associated with atrial fibrillation in rheumatic mitral stenosis. Asian Cardiovasc Thorac Ann 2015;23(1):17-23. [Crossref]

27. Ancona R, Comenale Pinto S, Caso P, Di Salvo G, Severino S, D'Andrea A, et al. Two-dimensional atrial systolic strain imaging predicts atrial fibrillation at 4-year follow-up in asymptomatic rheumatic mitral stenosis. J Am Soc Echocardiogr 2013;26(3):270-7. [Crossref]

28. Kawakami H, Ramkumar S, Nolan M, Wright L, Yang H, Negishi K, et al. Left atrial mechanical dispersion assessed by strain echocardiography as an independent predictor of new-onset atrial fibrillation: A case-control study. J Am Soc Echocardiogr 2019;32(10):1268-76.e3. [Crossref]

29. Degiovanni A, Bortnik M, Dell'Era G, Bolzani V, Occhetta E, Bellomo G, et al. Analysis of electrical and mechanical left atrial properties in patients with persistent atrial fibrillation. Int J Cardiovasc Imaging 2013;29(1):71-8. [Crossref]

30. Kupczynska K, Michalski BW, Miskowiec D, Kasprzak JD, Szymczyk E, Wejner-Mik P, et al. Incremental value of left atrial mechanical dispersion over CHA2DS2-VASc score in predicting risk of thrombus formation. Echocardiography 2018;35(5):651-60. [Crossref]

31. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J 2022;43(7):561-632. [Crossref]

Triglyceride-Glucose Index Could be Used to Predict Severity of Coronary Artery Ectasia

Ersan Oflar[1](İD), İsmail Ünğan[2](İD), Cennet Yıldız[1](İD), Güngör İlayda Bostancı Alp[1](İD), Büşra Mavi[1](İD), Fatma Nihan Turhan Çağlar[1](İD), Demet Erciyes[3](İD), Alparslan Şahin[1](İD)

[1] Clinic of Cardiology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Türkiye
[2] Clinic of Cardiology, Yalova State Hospital, Yalova, Türkiye
[3] Department of Cardiology, Demiroğlu Science University Faculty of Medicine, İstanbul, Türkiye

ABSTRACT

Introduction: Coronary artery ectasia (CAE) refers to a 1.5 fold increase in coronary artery diameter compared to the normal segment. Although the underlying pathophysiological mechanism is not fully elucidated, coronary atherosclerosis is thought to play a role in more than half of the cases. Triglyceride glucose (TyG) index is an indicator of insulin resistance. In the present study, aimed to evaluated TyG index values in CAE cases and find if a predictive value of TyG index existed.

Patients and Methods: Sixty-one patients with CAE (study group) and 64 patients with normal coronary arteries (control group) were included in the study. TyG index was calculated as ln (fasting triglyceride × fasting glucose/2).

Results: There were no differences between the two groups with respect to age, sex, diabetes mellitus prevalence, and biochemical parameters including, white blood cell, platelet, lymphocyte, monocyte counts, hemoglobin, hematocrit, urea, glucose, total cholesterol, high density lipoprotein-cholesterol, triglyceride levels and TyG index value. Twenty-five patients (41.0%) had one-vessel involvement, 24 (39.3%) patients had two-vessel involvement and 12 (19.7%) patients had three-vessel involvement. Right coronary artery was the most commonly affected vessel (11, 44%), followed by left anterior descending artery (8, 35%), left main coronary artery (4, 16%) and circumflex artery (1, 4%). TyG index was statistically significantly higher in patients who had two/three vessel involvement (8.80 ± 0.48 vs 9.14 ± 0.62, p= 0.027). TyG index had statistically significant correlation with the number of ectatic vessels (r= 0.275, p= 0.032). ROC curve analysis showed that TyG index was useful for the prediction of ectasia severity (AUC= 0.653, 95% CI= 0.515-0.792, p= 0.043). TyG index value of 9.16 had 41.7% sensitivity and 84% specificity for prediction of CAE severity.

Conclusion: TyG index, which is easily calculated from biochemical parameters, might be used for the assessment of CAE severity.

Key Words: Triglyceride; glucose; index; coronary arteries; ectasia

Trigliserid Glukoz İndeksi Koroner Arter Ektazi Ciddiyetinin Değerlendirilmesinde Kullanılabilir Bir Ölçektir

ÖZET

Giriş: Koroner arter ektazisi (KAE), normal segmente göre koroner arter çapında 1.5 kat artışı ifade eder. Altta yatan patofizyolojik mekanizma tam olarak aydınlatılmış olmasa bile vakaların yarısından fazlasında koroner aterosklerozun rol oynadığı düşünülmektedir. Trigliserid glukoz (TyG) indeksi insülin direncini gösteren bir belirteçtir. Bu çalışmada KAE olan hastalarda TyG indeks değerlerinin araştırılması amaçlandı.

Hastalar ve Yöntem: KAE olan 61 hasta ile normal koroner arteri olan 64 kontrol çalışmaya alındı. TyG indeksi ln (açlık trigliserid × açlık glukoz/2) formülü kullanılarak hesaplandı.

Bulgular: Her iki grup arasında yaş, cinsiyet, diyabetes mellitus prevalansı, lökosit, trombosit, lenfosit, monosit sayıları, hemoglobin, hematokrit, üre, glukoz, total kolesterol, yüksek yoğunluklu lipoprotein kolesterol, trigliserid seviyeleri ve TyG indeksi değeri açısından fark gözlenmedi. En sık etkilenen damar sağ koroner arterdi (%11, 44), bunu sol ön inen arter (%8, 35), sol ana koroner arter (%4, 16) ve sirkumfleks arter (%1.4) izledi. İki ve üç damar tutulumu gösteren hastaların TyG indeks değerleri kontrol grubuna göre anlamlı olarak yüksekti (8.80 ± 0.48, 9.14 ± 0.62, p= 0.027). TyG indeksinin ektazi gösteren damar sayısı ile korelasyon gösterdiği saptandı (r= 0.275, p= 0.032). ROC eğrisi analizi TyG indeks 9.16 değerinin KAE'sinin %41.7 duyarlılık ve %84 özgüllük ile predikte ettiğini gösterdi. (Eğri altında kalan alan (AUC)= 0.653, %95 güven aralığı= 0.515-0.792, p= 0.043).

Sonuç: TyG indeks KAE ciddiyetini göstermede yararlı olabilecek basit bir biyokimyasal parametredir.

Anahtar Kelimeler: Trigliserid; glukoz; indeks; koroner arter; ektazi

Cite this article as: Oflar E, Ünğan İ, Yıldız C, Bostancı Alp Gİ, Mavi B, Turhan Çağlar FN, et al. Triglyceride-glucose index could be used to predict severity of coronary artery ectasia. Koşuyolu Heart J 2023;26(1):34-39.

Correspondence

Cennet Yıldız

E-mail: cennet_yildiz@live.com
Submitted: 27.10.2022
Accepted: 06.02.2023
Available Online Date: 21.03.2023

INTRODUCTION

Coronary artery ectasia (CAE) is described as 1.5 fold dilatation of coronary artery segment relative to adjacent normal coronary artery[1]. Its prevalence differs according to the diagnostic modality used. Estimated angiographic prevalence of CAE ranges between 1 to 5%; however, an Indian study has reported 10% incidence in patients with ischemic heart disease[2,3]. CAE has occurred with a frequency of 9.9% in Turkish patients having undergone cardiac catheterization. Although pathophysiological mechanisms underlying CAE have not been fully elucidated, almost half of cases has been attributed to coronary atherosclerosis. Other etiologies for CAE include inflammatory and connective tissue diseases, congenital diseases and percutaneous interventions[4-6]. Markis et al. have shown that histopathological changes underlying CAE have similarities with atherosclerosis, suggesting a common mechanism[7]. Atherosclerosis usually begins as vascular thickening without causing stenosis (positive remodeling). Enlargement of the artery mainly occurs towards external elastic lamina giving a false impression of normal luminal diameter[8]. In this regard, CAE could be considered as a form of positive remodeling. Chronic exposure to herbicides, vasodilator substances, anabolic steroid use, alterations of angiotensin converting enzyme gene, abnormal vessel metabolism are other probable causes of CAE[9-11]. Right coronary artery (RCA) is the most commonly affected artery, followed by left anterior descending artery (LAD) and circumflex artery (Cx)[2]. Concomitant coronary artery stenosis is usually present in 80% to 90% of CAE cases, and if it occurs without coronary artery disease, it is called isolated CAE[12,13]. According to its morphology, CAE can be classified into two forms: saccular (longitudinal diameter is less than transverse diameter) or fusiform (longitudinal diameter is greater than transverse diameter). Sluggish flow in the ectatic segments may cause angina pectoris, acute coronary syndrome, thrombus formation, embolization, and congestive heart failure[14,15].

There is ample scientific evidence demonstrating increased risk of atherosclerosis in patients with insulin resistance (IR) even without presence of hyperglycemia[16]. Proinflammatory cytokine secretion, impaired insulin signaling in peripheral tissues, dyslipidemia with resultant endothelial dysfunction could promote formation of atherosclerotic lesions[17]. Since measurement of IR usually requires sophisticated techniques, simpler methods have been sought in clinical practice. Most commonly used method for quantification of IR is homeostasis model assessment -estimated insulin resistance (HOMA-IR), which is relatively expensive and requires measurement of both serum glucose and insulin levels. Hyperglycemia and hypertriglyceridemia are the predominant laboratory abnormalities in insulin resistant patients. Triglyceride glucose index (TyG index), which is calculated from fasting triglyceride and glucose concentrations, has been proposed as a simple and reliable marker for the screening of IR. Its predictive value has been shown in various diseases including acute myocardial infarction, atherosclerosis, hypertension (HT) and diabetes mellitus (DM)[18-21]. To the best of our knowledge, no study has investigated the value TyG index in patients with CAE. Since atherosclerosis plays role in pathogenesis of CAE, we hypothesize that TyG index is increased in patients with CAE. Therefore, the aim of the present study was to evaluate TyG index values in isolated CAE cases and to find if a predictive value of TyG index existed.

PATIENTS and METHODS

In this single-center, retrospective study, we evaluated the coronary angiographies of patients who had undergone diagnostic coronary angiography in our clinic between January 2018 and January 2020. A total of 10.843 coronary angiographic recordings of the patients were screened, 545 patients had both CAE and coronary artery stenosis of more than 50%, 61 patients had isolated CAE. Demographic and clinical characteristics of the patients were obtained from electronic data files. Sixty-one patients with CAE and 64 age and sex-matched controls were included in the study. Study and control groups consisted of patients with CAE and normal coronary arteries, respectively. Since coronary artery stenosis more than 50%, acute coronary syndromes, congestive heart failure, valvular heart disease, malignancy, renal/hepatic failure, inflammatory diseases might have impact on TyG index, these patients were excluded from the study. Local ethics committee approved the study, and it was conducted in accordance with the declaration of Helsinki.

After an overnight fast, blood samples were collected from antecubital fossa using venipuncture method. Biochemical parameters including urea, creatinine, glomerular filtration rate (GFR), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglyceride (TG), white blood cell count (WBC), hemoglobin (Hgb), hematocrit (Hct), platelet count (Plt), red cell distribution width (RDW), lymphocyte and monocyte counts were assessed. TyG index was calculated as ln (fasting triglyceride × fasting glucose/2)[22]. DM was described as fasting glucose ≥126 mg/dL or taking antidiabetic medication. HT was diagnosed when patient's systolic and/or diastolic blood pressures were greater than 140 and 90 mmHg, respectively or use of antihypertensives. Hyperlipidemia was described as TC ≥200 mg/dL or taking anti-lipidemic medication. Diagnosis of CAE was made by coronary angiography. Coronary angiographies of the study population were assessed by two experienced cardiologists blinded to the patient's data. CAE was described as more than 50% dilatation of a coronary segment relative to the normal segment. Mild involvement by CAE was described as diffuse or segmental ectasia of one vessel. If the patient had diffuse involvement of two/three vessels or diffuse involvement of one

vessel with segmental involvement of another, that was considered as severe involvement.

Primary outcome of the study was to evaluate if there was a difference in TyG index values in patients with CAE and normal coronary arteries. Secondary outcomes of the study were to find the incidence of CAE and its correlation with TyG index.

Statistical Analysis

Normality of the data was tested by Kolmogorov-Smirnov test. Parametric and non-parametric variables were expressed as mean ± SD and median (min-max), respectively. Based on previous studies results, we found that the effect size for this study was 0.75. In order to evaluate differences between the two groups with an alpha value of 0.05 and power of 80%, the required sample size was 23 subjects per group. For comparison of two groups, Mann-Whitney U test and independent samples t-test were used. Correlation of TyG index with the number of ectatic vessels was done by Spearman correlation analysis. Receiver operating characteristic (ROC) curve analysis was used to select optimal threshold of TyG index for the prediction of CAE. Independent predictors of CAE severity were assessed by univariate logistic regression analysis. All analyses were conducted by Statistical Package for Social Sciences (version 25, USA).

RESULTS

Mean ages of the study and control groups were 55.5 (28-77) and 54 (23-74) years, respectively (p= 0.538). There were no differences between the two groups with respect to sex, DM prevalence, biochemical parameters including, WBC, Plt, lymphocyte, monocyte counts, Hgb, Hct, urea, glucose, TC, HDL-C, TG levels, and TyG index value. The number of hypertensive patients was found to be higher in the study group as compared to the control group. In addition, RDW, GFR and creatinine levels were higher in the study group than those of the control group (Table 1).

Table 1. Clinical and biochemical characteristic of the groups

Parameter	Control Group (n= 59)	Study Group (n= 61)	p
Age (years)	54 (23-74)	55.5 (28-77)	0.538
Sex			0.331
Female (n, %)	22 (37.3)	17 (27.9)	
Male (n, %)	37 (62.7)	44 (72.1)	
HT (n, %)	22 (34.9)	41 (65.1)	0.001
DM (n, %)	11 (40.7)	16 (59.3)	0.343
Hgb (g/dL)	13.62 ± 1.66	13.49 ± 1.52	0.648
WBC ($10^3/\mu$L)	7.89 (4.11-18.51)	7.52 (3.6-14.4)	0.674
Hct (%)	40.57 ± 4.06	4.17 ± 4.32	0.436
Plt ($\times10^9$/l)	269 (86-529)	252 (160-437)	0.398
RDW (%)	13.2 (11.9-20.7)	13.95 (12.2-22.7)	0.000
Lymphocyte ($10^3/\mu$L)	2.49 (1.22-5.04)	2.11 (0.9-4.4)	0.131
Monocyte ($10^3/\mu$L)	0.57 (0.31-1.09)	0.59 (0.24-1.36)	0.603
Urea (mg/dL)	31 (18-87)	31 (16-100)	0.725
Creatinine(mg/dL)	0.74 (0.42-2.33)	0.87 (0.51-2.07)	0.004
GFR (mL/min/1.73m^2)	97.59 ± 19.58	76.43 ± 19.64	0.001
Glucose (mg/dL)	99 (70-399)	98 (76-284)	0.975
TC (mg/dL)	216.09 ± 47.26	197 ± 42.97	0.074
HDL-C (mg/dL)	44 (22-98)	41 (25-75)	0.224
TG (mg/dL)	138.5 (46-904)	156 (39-824)	0.634
LDL-C (mg/dL)	133 (70-400)	120 (54-210)	0.047
TyG index	8.88 (7.66-12.10)	8.97 (7.71-10.93)	0.714

HT: Hypertension, DM: Diabetes mellitus, Hgb: Hemoglobin, WBC: White blood cell, Hct: Hematocrit, Plt: Platelet, RDW: Red blood cell distribution width, GFR: Glomerular filtration rate, TC: Total cholesterol, HDL-C: High density lipoprotein cholesterol, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, TyG: Triglyceride glucose index.

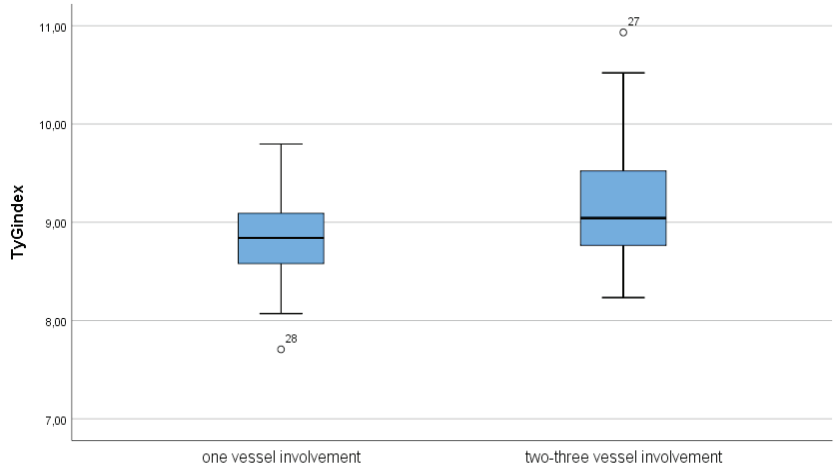

Figure 1. TyG index values of patients who had one vessel and two-three vessel CAE.

Twenty-five patients (41.0%) had one-vessel involvement, 24 (39.3%) patients had two-vessel involvement and 12 (19.7%) patients had three-vessel involvement. Of the patients who had one vessel involvement, RCA was the most commonly affected vessel (11, 44%), followed by LAD (8, 35%), left main coronary artery (LMCA) (4, 16%) and Cx (1, 4%). When we analyzed all CAE patients without considering the number of vessel involvement, the frequency of the affected vessel, in decreasing order, was LAD (39, 63.9%), RCA (33, 54.1%), Cx (28, 45.9%), and LMCA (9, 14.8%).

When patients who had one-vessel involvement and two/three-vessel involvement were compared, it was found that TyG index was statistically significantly higher in patients who had two/three vessel involvement (8.80 ± 0.48 vs 9.14 ± 0.62, p= 0.027) (Figure 1). Furthermore, TyG index of the patients who had two-three vessel CAE was significantly higher compared to the patients who had normal coronary arteries (9.27 ± 0.67 vs 9.00 ± 0.84, p= 0.034). Since the number of HT patients was found to be higher in the study group, we also analyzed the number of HT patients in one-vessel CEA involvement with two/three-vessel CAE involvement. We did not find any differences with respect to HT between one-vessel involvement and two/three-vessel involvement (n= 14, 56% vs n= 27, 75%, respectively, p= 0.121). According to correlation analysis, TyG index had statistically significant but a weak correlation with the number of ectatic vessels (r= 0.275, p= 0.032). ROC curve analysis showed that TyG index was useful for the prediction of two/three vessel involvement (AUC= 0.653, CI 95%= 0.515-0.792, p= 0.043) (Figure 2). TyG index value of 9.16 had 41.7% sensitivity and 84% specificity for the prediction of ectasia severity. According to logistic regression analysis, TyG index and the presence of DM were independent predictors of CAE severity (involvement of two/three vessels) (for DM, OR= 4.145, p= 0.044, 95% CI= 1.038-16.555 and for TyG index, OR= 3.167, p= 0.035, 95% CI= 1.082-9.267).

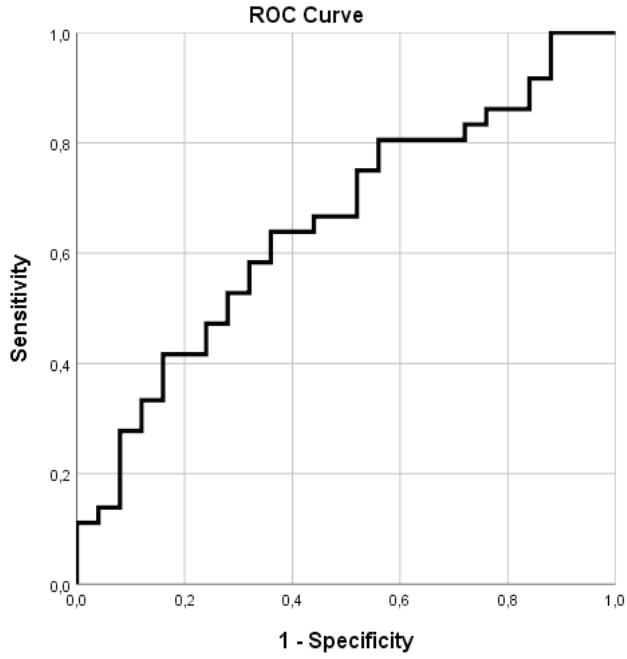

Figure 2. ROC curve analysis for prediction of CAE severity.

DISCUSSION

Our study showed that although TyG index was not different between patients who had normal and ectatic coronary arteries, patients with more diffuse involvement of ectasia had higher values of TyG index compared patients who had normal coronary arteries. TyG index could be useful in the prediction of the severity of coronary involvement in patients with CAE.

CAE is predominantly found in males with a male to female ratio of 3:1[23]. In the present study, 72.1% of the patients was male and LAD was the most commonly affected vessel. Although RCA has been reported to be the most frequently affected vessel in most of the studies, some studies have found different findings. Sultana et al. and Malviya et al. have found similar findings to our study, with the involvement of LAD in 63% and 59.6% of the cases, respectively[24,25]. In our study, 41% cases had single-vessel CAE, which is also in line with the previous studies[25].

The exact cause and pathophysiology of CAE is not fully understood; however, a variety of disorders including atherosclerosis, inflammatory diseases, connective tissue diseases, iatrogenic mechanisms and congenital causes have been reported to be associated with it. Several biochemical parameters have been investigated in order to determine risk factors and etiologic mechanisms underlying the disease process. Among laboratory parameters, we found that RDW and creatinine were significantly higher, whereas GFR was significantly lower in CAE patients. RDW has strong association with cardiovascular mortality and has been shown to be increased in CAE cases[26]. Yet, precise connection between CAE and increased RDW values has not been identified, factors that influence red blood cell homeostasis such as inflammation and oxidative stress might be the underlying link between two conditions[27,28]. Similarly, abnormalities in renal function are associated with CAE. Turkmen et al. have demonstrated that urinary excretion of albumin is increased in patients with CAE representing generalized condition that affects multiple tissues[29].

Insulin resistance can be considered as a syndrome which increases the risk of cardiovascular disease[30]. It appears to be related with dyslipidemia, hypertension, hypercoagulability, low-grade inflammation and other abnormalities. Zhang et al. have demonstrated that patients with CAE have higher insulin levels suggesting a common pathway in pathogenesis of CAE. In their study, magnitude of the lesions differed significantly among patients, patients with higher insulin levels had more severe disease[31]. This may be attributed to endothelial dysfunction, fat deposition in arterial wall, accelerated atherosclerosis and development of CAE[32]. Cao et al. have compared fasting insulin levels and HOMA-IR indices of patients with CAE, arteriosclerosis and normal coronary arteries. In their study, fasting insulin and HOMA-IR levels were significantly higher compared to that of patients with arteriosclerosis and normal coronary arteries. They have also found positive correlations between fasting glucose and HOMA-IR levels and the severity of CAE[33]. In this context, CAE might be considered as exaggerated vascular remodeling in response to atherosclerotic lesions[34].

TyG index is a simple calculation obtained from fasting glucose and TG levels. It is proposed as a surrogate marker for insulin resistance[35]. Since insulin resistance might play a role in the development of CAE, in our study, we wanted to measure TyG index values of CAE patients. We did not find any differences in TyG index values between the patient and control group. However, when patients who had two/three vessel involvement were compared with control group and patients with one vessel involvement, we found significant differences. These findings suggested that mild disease had only marginally elevated TyG index levels that did not reach statistical significance. According to our results, TyG index could be used to assess CAE severity. It was positively correlated with the number of CAE vessels. Moreover, patients with two/three-vessel involvement had higher TyG index values compared to controls. Our results also supported the hypothesis that insulin resistance and atherosclerosis were the part of the mechanism underlying the pathogenesis of CAE.

CONCLUSION

In conclusion, TyG index might be used in the assessment of severity of CAE. Its calculation is very easy and could be readily used in daily clinical practice. Large scale studies are needed to evaluate the value of TyG index in CAE patients.

Limitations

It was a single-center study with a relatively small sample size. Plasma insulin and HOMA-IR levels of the patients were not measured. TyG index was only measured at baseline, more frequent measurement could give more information. Last, long term follow-up of the patients was not conducted.

Ethics Committee Approval: This study was approved by Bakırköy Dr. Sadi Konuk Research and Training Hospital Clinical Research Ethics Committee (Decision no: 2021-19-01, Date: 04.10.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - EO, İU, CY, AŞ; Analysis/Interpretation - CY, İBA, BM; Data Collection - EO, İU, AS; Writing - CY; Critical Revision - All of authors; Statistical Analysis - CY; Overall Responsibility - All of authors.

Conflict of Interest: The authors have no conflicts of interest to declare.

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

REFERENCES

1. Hartnell GG, Parnell BM, Pridie RB. Coronary artery ectasia, its prevalence and clinical significance in 4993 patients. Br Heart J 1985;54:392-5. [Crossref]
2. Manginas A, Cokkinos DV. Coronary artery ectasias: Too large to miss? Eur Cardiovasc Dis 2006;2:1-6. [Crossref]
3. Sharma SN, Kaul U, Sharma S, Wasir HS, Manchanda SC, Bahl VK, et al. Coronary arteriographic profile in young and old Indian patients with ischemic heart disease: A comparative study. Indian Heart J 1990;42:365-9.
4. Chaithiraphan S, Goldberg E, O'Reilly M. Multiple aneurysms of coronary artery in sclerodermal heart disease. Angiology 1973;24:86-93. [Crossref]
5. Shiro I, Bannerman RM, Graf CJ, Brennan JC. Ehlers-Danlos syndrome with multiple arterial lesions. Am J Med 1969;47:967-77. [Crossref]
6. Türkmen M, Bitigen A, Esen AM. Coronary artery ectasia. J Med Sci 2006;26:68-72.
7. Markis JE, Joffe CD, Cohn PF, Feen DJ, Herman MV, Gorlin R. Clinical significance of coronary arterial ectasia. Am J Cardiol 1976;37:217-22. [Crossref]
8. Antoniadis AP, Chatzizisis YS, Giannoglou GD. Pathogenetic mechanisms of coronary ectasia. Int J Cardiol 2008;130:335-43. [Crossref]
9. Sorrell VL, Davis MJ, Bove AA. Current knowledge and significance of coronary artery ectasia: A chronologic review of the literature, recommendations for treatment, possible etiologies, and future considerations. Clin Cardiol 1998;21:157-60. [Crossref]
10. Androulakis AE, Andrikopoulos GK, Kartalis AN, Stougiannos PN, Katsaros AA, Syrogiannidis DN, et al. Relation of coronary artery ectasia to diabetes mellitus. Am J Cardiol 2004;93:1165-7. [Crossref]
11. Johanning JM, Franklin DP, Han DC, Carey DJ, Elmore JR. Inhibition of inducible nitric oxide synthase limits nitric oxide production and experimental aneurysm expansion. J Vasc Surg 2001;33:579-86. [Crossref]
12. Swaye PS, Fisher LD, Litwin P, Vignola PA, Judkins MP, Kemp HG, et al.Aneurysmal coronary artery disease. Circulation 1983;67:134-8. [Crossref]
13. Sadr-Ameli M, Sharifi M. The natural history of ectatic coronary artery disease. Iranian Heart J 2001;2:12-6.
14. Mrdović I, Jozić T, Asanin M, Perunicić J, Ostojić M. Myocardial reinfarction in a patient with coronary ectasia. Cardiology 2004;102:32-4. [Crossref]
15. Kühl M, Varma C. A case of acute coronary thrombosis in diffuse coronary artery ectasia. J Invasive Cardiol 2008;20:23-5.
16. DeFronzo RA. Insulin resistance, lipotoxicity, type 2 diabetes and atherosclerosis: The missing links. The Claude Bernard Lecture. Diabetologia 2010;53:1270-87. [Crossref]
17. Bornfeldt KE, Tabas I. Insulin resistance, hyperglycemia, and atherosclerosis. Cell Metabol Rev 2011;14:575-85. [Crossref]
18. Zhang Y, Ding X, Hua B, Liu Q, Gao H, Chen H, et al. Predictive effect of triglyceride glucose index on clinical events in patients with type 2 diabetes mellitus and acute myocardial infarction: Results from an observational cohort study in China. Cardiovasc Diabetol 2021;20:43. [Crossref]
19. Chiu TH, Tsai HJ, Chiou HYC, Wu PY, Huang JC, Chen SC. A high triglyceride-glucose index is associated with left ventricular dysfunction and atherosclerosis. Int J Med Sci 2021;18:1051-7. [Crossref]
20. Zheng R, Mao Y. Triglyceride and glucose (TyG) index as a predictor of incident hypertension: A 9-year longitudinal population-based study. Lipids Health Dis 2017;16:175. [Crossref]
21. Srinivasan S, Singh P, Kulothungan V, Sharma T, Raman R. Relationship between triglyceride glucose index, retinopathy and nephropathy in type 2 diabetes. Endocrinol Diabetes Metab 2020;4:e00151. [Crossref]
22. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 2010;95:3347-51 [Crossref]
23. Lin CT, Chen CW, Lin TK, Lin CL. Coronary artery ectasia. Tzu Chi Med J 2008;20:270-4. [Crossref]
24. Sultana R, Sultana N, Ishaq M, Samad A. The prevalence and clinical profile of angiographic coronary ectasia. J Pak Med Assoc 2011;61:372-5.
25. Malviya A, Jha PK, Mishra A. Isolated coronary artery ectasia; clinical, angiographic, and follow up characteristics. Indian Heart J 2017;69:619-23. [Crossref]
26. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJV, Pfeffer MA, et al. Red cell distribution width as a novel prognostic marker in heart failure: Data from the CHARM program and the Duke Databank. Am Coll Cardiol 2007;50:40-7. [Crossref]
27. Sezen Y, Bas M, Polat M, Yildiz A, Buyukhatipoglu H, Kucukdurmaz Z, et al. The relationship between oxidative stress and coronary artery ectasia. Cardiol J 2010;17:488-94.
28. Guo YL, Luo SH, Tang Y, Li JJ. Association of red cell distribution width with the presence of coronary artery ectasia. Clin Lab 2014;60:199-205. [Crossref]
29. Turkmen S, Yolcu M, Cagliyan CE, Sercelik A, Ipek E, Tekin K, et al. The relationship between microalbuminuria and isolated coronary artery ectasia. Eur Rev Med Pharmacol Sci 2014;18:1661-5.
30. Ginsberg HN. Insulin resistance and cardiovascular disease. J Clin Invest 2000;106:453-8. [Crossref]
31. Zhang X, Liu A, Guo M, Guan J, Cai S, Du Q, et al. Correlations among plasma insulin concentration, insulin sensitivity and coronary artery ectasia. Int J Clin Exp Med 2018;11:2325-30
32. Pino AD, DeFronzo RA. Insulin resistance and atherosclerosis: Implications for insulin-sensitizing agents. Endocr Rev 2019;40:1447-67. [Crossref]
33. Cao Y, Yin H, Yin H, Jiang Z, Wang T, Chen T. Associations of the insulin level and insulin resistance with the severity of coronary artery ectasia. Int J Clin Exp Med 2018;11:4937-42.
34. Devabhaktuni S, Mercedes A, Diep J, Ahsan C. Coronary artery ectasia-a review of current literature. Curr Cardiol Rev 2016;12:318-23. [Crossref]
35. Hong S, Han K, Park CY. The triglyceride glucose index is a simple and low-cost marker associated with atherosclerotic cardiovascular disease: A population-based study. BMC Med 2020;18:361. [Crossref]

Percutaneous Treatment of Pulmonary Valvular Stenosis and Secundum Type Atrial Septal Defect in a Young Adult

Ahmet Emir Ulutaş(İD), Serkan Kahraman(İD), Gamze Babur Güler(İD), Arda Can Doğan(İD), Mustafa Yıldız(İD)

Clinic of Cardiology, Thoracic and Cardiovascular Surgery Center, University of Health Sciences Mehmet Akif Ersoy Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Pulmonary valve stenosis (PS) and secundum type atrial septal defect (ASD) are common forms of congenital heart disease. While traditional treatment for PS and ASD is open surgery, percutaneous treatment of both diseases are widely used with high rates of success and lower complication. However, the combination of PS with ASD in the same patient is relatively rare, and the optimal strategy is debated. We performed consecutive percutaneous balloon pulmonary valvuloplasty and ASD occlusion in a young adult patient with severe congenital PS associated with a secundum ASD.

Key Words: Atrial septal defect; pulmonary valve stenosis

Genç Erişkinde Pulmoner Kapak Stenozu ve Sekundum Tip Atrial Septal Defektin Perkütan Tedavisi

ÖZET

Pulmoner kapak stenozu (PS) ve sekundum tip atrial septal defekt (ASD), konjenital kalp hastalıklarının genel formlarıdır. PS ve ASD'nin geleneksel tedavisi açık cerrahi iken, her iki hastalığın da perkütan tedavisi yüksek başarı oranları ve daha düşük komplikasyon oranları ile yaygın olarak kullanılmaktadır. Ancak aynı hastada PS ile ASD kombinasyonu nispeten nadirdir ve optimal stratejisi tartışmalıdır. Vakamızda sekundum ASD ile ilişkili şiddetli konjenital PS'si olan genç erişkin bir hastada ardışık perkütan balon pulmoner valvüloplasti ve ASD kapatması gerçekleştirdik.

Anahtar Kelimeler: Atriyal septal defekt; pulmoner kapak stenozu

INTRODUCTION

Among congenital heart diseases, pulmonary valve stenosis (PS) and secundum type atrial septal defect (ASD) are more common than others. ASD and PS were treated as open surgery in the past. Nowadays, transcatheter interventional therapy of ASD and PS are performed with high success rates[1-5]. However, the combination of PS with ASD in the same patient is relatively rare, and the optimal strategy is debated. We performed consecutive percutaneous balloon pulmonary valvuloplasty (PBPV) and ASD occlusion in a young adult patient with severe congenital PS associated with a secundum type ASD.

CASE REPORT

A 22-year-old male patient followed up with known pulmonary valve stenosis was admitted to our hospital with dyspnea and worsening exercise intolerance. Physical examination revealed systolic ejection murmur (grade 3) at the mesocardiac and pulmonary area. Electrocardiography showed sinus tachycardia with incomplete right bundle branch block. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) revealed ejection fraction as 60%, dilated right chamber sides of heart, secundum type atrial septal defect (ASD) and severe pulmonary valve stenosis (max gradient: 74 mmHg). First, we planned to perform right heart catheterization (RHC) to verify pulmonary valve gradient and measure pulmonary vascular resistance. Then RHC was performed via the right femoral vein. In RHC, peak to peak pulmonary valve gradient was 70 mmHg, and PVR was 2 Wood units, with mean pulmonary artery pressure as 15 mmHg. Then in the same procedure, we

Cite this article as: Ulutaş AE, Kahraman S, Güler GB, Doğan AC, Yıldız M. Percutaneous treatment of pulmonary valvular stenosis and secundum type atrial septal defect in a young adult. Koşuyolu Heart J 2023;26(1):40-42.

Correspondence

Serkan Kahraman

E-mail: serkankahraman_86@outlook.com
Submitted: 05.11.2022
Accepted: 13.12.2022
Available Online Date: 21.03.2023

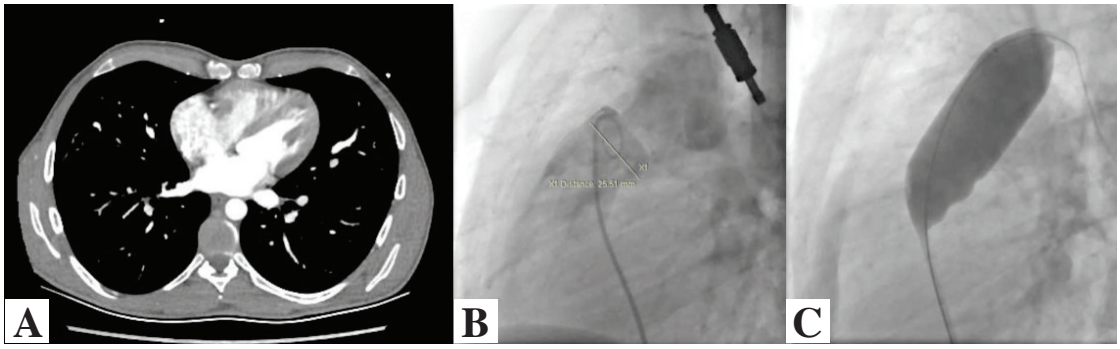

Figure 1. A. Computed tomographic image at the level of the pulmonary valve. **B.** Angiographic image of the pulmonary valve. **C.** Percutaneous balloon pulmonary valvuloplasty with a 2.5 x 15 mm pulmonary balloon.

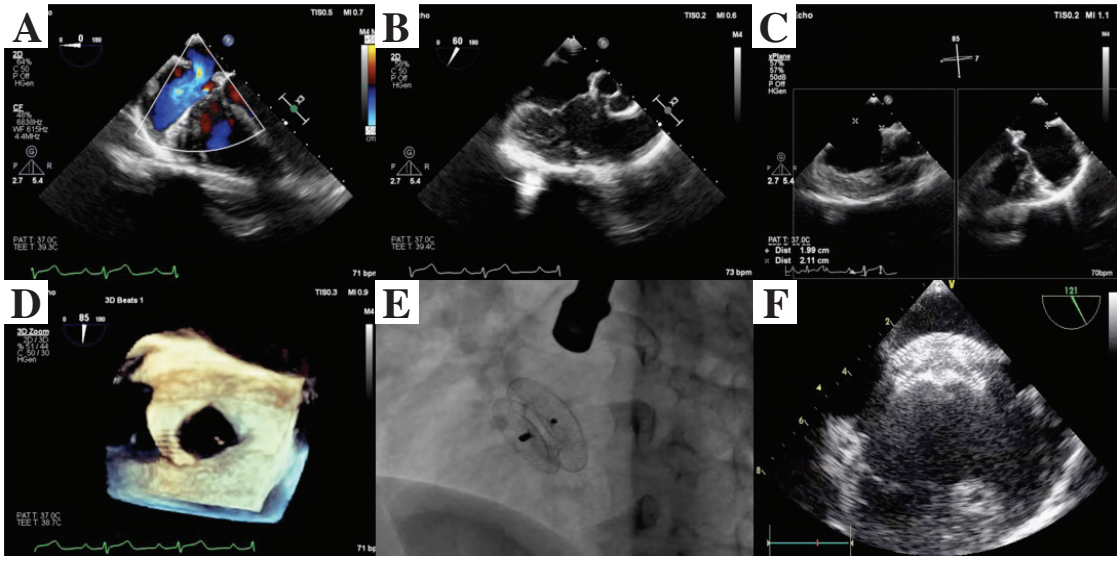

Figure 2. A-C. Transesophageal echocardiography imaging of the atrial septal defect. **D.** 3D transesophageal echocardiography imaging of the atrial septal defect. **E.** Angiographic image after percutaneous ASD closure. **F.** Transesophageal echocardiography imaging after atrial septal defect closure.

decided to perform PBPV. A pigtail catheter was placed in distal left pulmonary artery. Amplatz Superstiff wire was advanced through the pigtail to the distal pulmonary artery. The pigtail catheter was withdrawn, and a 2.5 × 15 mm pulmonary balloon was inflated in the appropriate position on the pulmonary valve. The procedure was terminated without any complications. Control TTE examination was performed after the procedure. There was a mild pulmonary regurgitation, and maximum gradient of the pulmonary valve was detected 18 mmHg. TEE examination was performed a month later after the procedure. Twenty-one mm secundum type ASD with a significant left to right shunt and mild pulmonary regurgitation were observed. Percutaneous ASD closure was planned to perform. The right femoral vein was cannulated with 6F sheath. A multipurpose catheter and hydrophilic guidewire were advanced through from the right atrium to the left atrium and left upper pulmonary vein. The Amplatz Superstiff wire was advanced in the pulmonary vein and the multipurpose catheter was removed. MemoPart occluder delivery system was advanced to the left atrium over the Amplatz Superstiff wire. Afterwards, a complete device occlusion of ASD was performed with a 22-mm Amplatzer septal occluder device. The patient was discharged from the hospital without any complications one day after the procedure, and is still followed up as asymptomatic.

DISCUSSION

The valvular type of PS is generally associated with ASD. The main pathological change of this disease is obstruction of the outflow tract of the right ventricle. When these two conditions are present simultaneously in a patient, a significant left-to-right shunt from ASD is often blocked due to the increased right ventricular pressure that originates from the outflow tract obstruction. It results in nearly normal pulmonary vascular pressure until adulthood[6,7]. Nowadays, percutaneous intervention techniques have become the method of choice for the treatment of these abnormalities in all age groups. PBPV

has become the initial choice for the treatment of PS in all age groups. When we look at the literature, we see two different approaches for transcatheter implementation. One of them is a combined approach in PBPV and ASD closure[8,9]. The other one is sequential PBPV and ASD closure. There is no clear consensus on this issue. Significant left to right shunt can increase pulmonary valvular gradient and results in pseudo-severe pulmonary stenosis. Thus, before performing PBPV, we should be sure that the valvular PS is clearly severe. On the other hand, severe PS can result in right to left shunt from ASD due to the increased right ventricle pressure. After performing PBPV, direction of the shunt and pulmonary vascular resistance should be evaluated carefully. In addition to having high success and long term clinical follow- up of both ASD closure and PBBV seperately, simultaneous procedures may be preferred compared to two-stepped procedures in the future. When we confirm combined adult congenital heart diseases and exclude pseudo-severe pulmonary stenosis, we need to consitute a specific algorithm in order to ensure cost-efectiveness and lower complication rates. After performing PBBV successfully ,we may have a opportunity to close ASD with the guidance of TEE and RHC at the same session. On the other hand, operator experience is quite important and requires more clinical cases. However,there are not enough clinical series regarding this issue. In our patient, we evaluated valvular PS as severe with the help of TEE, computed tomography and RHC. After performing PBPV, we performed RHC again and detected a significant left to right shunt from ASD with a low PVR. Then we performed percutaneous ASD closure. However, comparative studies are needed on this subject. During the procedure, whether or not there is any difference between the two groups in terms of complications should be checked. At the same time, it should be checked if there is any difference in the short and long-term clinical results between these two stepped or simultaneous procedures. We think that large-scale studies are needed to evaluate long-term results of different percutanoeus treatment modalities.

CONCLUSION

Percutaneous treatment of PS and ASD are widely used with higher success and lower complication rates. However, the management of combined adult congenital heart diseases is still controversial. Combined treatment may be performed simultaneously or as stepped procedures. According to patient characteristics and clinical determinants, there is still no consensus about optimal percutaneous treatment strategies.

Informed Consent: Written informed consent was obtained from patient who participated.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - All of authors; Analysis/Interpretation - All of authors; Data Collection - All of authors; Writing - All of authors; Critical Revision - All of authors; Final Approval - All of authors; Overall Responsibility - All of authors.

Conflict of Interest: All authors declare that they do not have conflict of interest.

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

REFERENCES

1. Kan JS, White Jr RI, Mitchell SE, Gardner TJ. Percutaneous balloon valvuloplasty: A new method for treating congenital pulmonary-valve stenosis. N Engl J Med 1982;307:540-2. [Crossref]
2. Saad MH, Roushdy AM, Elsayed MH. Immediate- and medium-term effects of balloon pulmonary valvuloplasty in infants with critical pulmonary stenoses during the first year of life: A prospective single center study. J Saudi Heart Assoc 2010;22:195-201. [Crossref]
3. Luo F, Xu WZ, Xia CS, Shi LP, Wu XJ, Ma XL, et al. Percutaneous balloon pulmonary valvuloplasty for critical pulmonary stenosis in infants under 6 months of age and short and medium term follow-up. Zhonghua Er Ke Za Zhi 2011;49:17-20.
4. Li H, Li YF, Li JJ, Shi JJ, Zhang ZW, Xu YM, et al. Short- and mid-term outcomes of transcatheter intervention for critical pulmonary stenosis and pulmonary atresia with intact ventricular septum in neonates. Zhonghua Er Ke Za Zhi 2012;50:925-8.
5. Ahmadi A, Sabri M. Percutaneous balloon valvuloplasty in patients with pulmonary valve stenosis: A single center experiment. J Pak Med Assoc 2012;62:58-61.
6. Carter JE Jr, Feldman T, Carroll JD. Sustained reversal of rightto-left atrial septal defect flow after pulmonic valvuloplasty in an adult. Eur Heart J 1994;15:575-6. [Crossref]
7. Kin H, Ishibashi Y, Tanabe K, Nakamura K, Matsumoto H, Okada S, et al. Effects of balloon pulmonary valvuloplasty on atrial shunting: A patient with pulmonary valve stenosis and a large secundum atrial septal defect. Jpn Circ J 1997;61:192-6. [Crossref]
8. Xu XD, Ding XY, Liu SX, Bai Y, Zhao XX, Qin YW. Immediate- and medium-term effects of simultaneous percutaneous corrections of secundum type atrial septal defect combined with pulmonary valve stenosis in local anesthesia and without transesophageal echocardiography guidance. J Cardiol 2015;65:32-6. [Crossref]
9. Wahl A, Windecker S, Misteli M, Meier B. Combined percutaneous pulmonary valvuloplasty and atrial septal defect closure for pulmonary valvular stenosis and associated secundum atrial septal defect in an adult. Catheter Cardiovasc Interv 2001;53:68-70. [Crossref]