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EDITORIAL TEAM

Scientific Reports in Medicine

- Adolescent Diseases
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- Physical Medicine and Rehabilitation
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- Mental Health and Diseases
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- Nuclear Medicine
- Oncological Diseases
- Sports Medicine
- Genetic Diseases
- Medical Pathology

The journal covers all relevant branches in human medicine specialties of the topics mentioned above.

Thank you for your interest in submitting your manuscript to Scientific Reports in Medicine for editing and publication consideration. In order to facilitate preparation and submission of your manuscript, we have prepared this guideline explaining basic points that should be taken into account when preparing the paper.

Scientific Reports in Medicine is a scientific publication of Academician Publishing and published three times a year online.

It is an open access scientific journal, which publishes original contributions in medical disciplines pertaining to human medicine. In this context, the Journal publishes original researches, case reports, and reviews based on clinical and experimental studies in all areas of human medicine. It is a scientific, periodic journal based on the principles of blind peer-review process. The publication language is English. The Journal is published online three times a year on April, August, and December.

Manuscripts submitted for publication in the journal should be prepared in accordance with research and publication ethics. All manuscripts submitted to the Journal are screened in terms of originality.

All manuscripts should be submitted by online system of the Journal.

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AUTHOR GUIDELINES

Subject areas include, but are not restricted to the clinical and experimental studies of the following fields: first aid and emergency medicine, family medicine, public health and preventive medicine, internal diseases, general surgery, gynecology and obstetrics, ear, nose and throat diseases, eye diseases, orthopedics and traumatology, radiology and radiodiagnostics, anesthesia and intensive care medicine, adolescent diseases, childhood diseases, multisystem diseases, physical medicine and rehabilitation, forensic medicine, mental health and diseases, cardiovascular system diseases, nervous system diseases, neurosurgery, respiratory system diseases, infectious diseases, occupational diseases, nuclear medicine, oncological diseases, sports medicine, genetic diseases, medical pathology.

The journal covers all relevant branches in human medicine specialties of the topics mentioned above.

Audience

Academicians, specialist physicians and research assistants in surgical and non-surgical medical disciplines and general practitioners.

Manuscript Preparation

All manuscripts which will be published in the journal must be in accordance with research and publication ethics. All authors should have contributed to the article directly either academically or scientifically. Presentations at congresses or in symposia are accepted only if they were not published in whole in congress or symposium booklets and should be mentioned as a footnote.

Manuscripts are received with the explicit understanding that they have not been published in whole or in part elsewhere, that they are not under simultaneous consideration by any other publication. Direct quotations, tables, or illustrations that have appeared in copyrighted material must be accompanied by written permission for their use from the copyright owner and authors. All articles are subject to review by the editors and referees.

Process of Peer Review

The journal utilizes a standard online site (SRINMED), operated by Academician Publishing, for the process of both manuscript submission and manuscript peer review. Upon receiving a manuscript submitted for consideration of publication to the journal, the journal manager and editorial staff review the submission to assure all required components as outlined in this Guide for Authors are included. The manuscript is then assigned to one of the co-editors (either the editor in chief or an associate editor) who directs and oversees the peer-review process. The co-editor then reviews the submission for relevance, content and quality. Those submissions deemed appropriate for consideration of publication are then assigned to at least two peer reviewers. In order for a manuscript to be considered for publication, it must be original and significant, providing a contribution to research and importance to field. In general, there should be no flaws in the specific procedures used in performance of the study, or in the logic used for the interpretation of the data. It is important that the results of the study support its conclusions, and that there are no errors in reference to prior work (or no exclusions of pertinent references). Where appropriate, confirmation of regulatory review (such as institutional review board approval) must be present. The validity of the statistics used (often including a justification of a sample size) to analyze data is necessary, and the data presented in the figures and tables should be reflective of the results presented and adequate to justify the study conclusions. In general, the manuscript length and quality of the writing are important to ensure its quality.

When the editor has a full complement of reviews completed, the editor reviews the comments and recommendations, and a decision regarding the suitability for publication of the manuscript is made. Acceptance is based on significance, and originality of the material submitted. If the article is accepted for publication, it may be subject to

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editorial revisions to aid clarity and understanding without changing the data presented.

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

About the scientific language to be used in writing your manuscript

In line with the recommendation of the international directories we applied to increase the scientific effectiveness of our journal and enrich its content, our Editorial Board has decided that the studies to be published in English. So the manuscripts sent to our journal are subject to English language control and revision.

Our experience from previous articles has shown that most of the articles prepared in English need to be improved in terms of fluent readability and intelligibility, as well as scientific and technical examination. Most of the manuscrpits should undergo a comprehensive review and revision process in terms of language, before they were included in the review stage.

Therefore, we recommend that you receive professional English editing and proofreading services before submitting your manuscript to our journal, although it is not mandatory.

You can contact Academician Publishing to receive Editing and Proofreading services for a fee. You can click here to contact Academician Publishing.

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By uploading the revised English full text of your manuscript to our Journal system by ensuring that English Editing and Proofreading is carried out by a local or foreign professional, you may minimize the possibility of rejection due to translation errors.

Use of first person

In addition, it is necessary to make the necessary checks and revisions in terms of language of your work and to ensure integrity in terms of language and time use throughout the entire article.

Expressions such as ... "Our study, in our study, we, we did, we found, we aimed, I did, I found, I think ... etc." should be revised as follows;

• In this study, … it was found/determined/… or

• In this study … it was aimed to …

Names made up of single word should not be abbreviated.

Instead of,

• Hypertension (HT) is one of the most …

Throughout the manuscript, you should use;

• Hypertension is one of the most …

Instead of,

• Rituximab (RTX) is an IgG1 kappa chimeric monoclonal

Throughout the manuscript, you should use;

• Rituximab is an …

Numbers should always be used to indicate statistics, age and measurements (including time as in the 3 weeks example). In specifying the others, only the numbers one to nine should be written in letters. (Numbers between 1-10 should be written with letters, except for the date and number of cases)

For example;

• In 2 studies, …

Should be replaced with;

• In two studies …

For example;

• … perivascular lymphotic infiltration in only 10 percent and fibrosis in 7 percent of the patients,

Should be replaced with;

• … perivascular lymphotic infiltration in only 10% of patients … in 7% of patients …

Prejudiced expressions should be avoided in expressions other than classical textbook knowledge, which has been verified by dozens of studies and has become the industry standard in the literature.

• determined to be high

Should be replaced with;

• … was found to be high.

Or throughout the entire manuscript;

• found to be significantly higher …

If diametrically opposite findings are mentioned among the studies mentioned in the Discussion section, it should be stated as "… a significant relationship was found /

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observed / reported", rather than "a significant relationship was determined" etc.

• While no significant relationship was determined between blood pressure and disease severity (26,27), a strong relationship was determined in some studies (28,29).

Should be replaced with;

While no significant relationship was observed between blood pressure and disease severity (26,27), it was reported that a strong relationship was found in some studies (28,29).

General Principles

The text of articles reporting original research should be divided into Introduction, Methods, Results [Findings], and Discussion sections. This so-called "IMRAD" structure is not an arbitrary publication format but a reflection of the process of scientific discovery. Articles often need subheadings within these sections to further organize their content. Other types of articles, such as meta-analyses, may require different formats, while case reports, narrative reviews, and editorials may have less structured or unstructured formats.

Electronic formats have created opportunities for adding details or sections, layering information, cross-linking, or extracting portions of articles in electronic versions. Supplementary electronic-only material should be submitted and sent for peer review simultaneously with the primary manuscript.

Sections

Abstract

Original research, systematic reviews, and meta-analyses require structured abstracts. The abstract should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study participants, settings, measurements, analytical methods), main findings (giving specific effect sizes and their statistical and clinical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations, note important limitations, and not overinterpret findings. Please, do not cite figures, tables or references in the abstract.

Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to ensure that they accurately reflect the content of the article. All the articles submitted to the journal require to include abstract in English. Abstracts of original articles should not exceed 250 words.

Keywords

Three to six words or determinative groups of words should be written below the abstract. Abbreviations should not be used as keywords. Keywords in English should be chosen from MESH (Medical Subject Headings http://www.nlm.nih.gov/mesh) index. Abbreviations cannot be used as keywords, but instead they should be written explicitly. Letters that do not exist in Latin alphabet (e.g. alpha, beta, delta etc.) should be used with their pronunciation.

Examples; carbon monoxide, firearms, sexual abuse, oral mucosa

Introduction

Provide a context or background for the study (that is, the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation. Cite only directly pertinent references, and do not include data or conclusions from the work being reported.

Methods

The guiding principle of the Methods section should be clarity about how and why a study was done in a particular way. The Methods section should aim to be sufficiently detailed such that others with access to the data would be able to reproduce the results.

The authors should clearly describe the selection of observational or experimental participants (healthy individuals or patients, including controls), autopsied persons, including eligibility and exclusion criteria and a description of the source population.

In general, the section should include only information that was available at the time the plan or protocol for the

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study was being written; all information obtained during the study belongs in the Results [Findings] section. If an organization was paid or otherwise contracted to help conduct the research (examples include data collection and management), then this should be detailed in the methods.

The Methods section should include a statement indicating that the research was approved or exempted from the need for review by the responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the Declaration of Helsinki should be included.

Identifying information, including names, initials, or autopsy numbers of the patients/deceased should not be exposed in written descriptions or photographs in no ways. Identifying details should be omitted if they are not essential.

Informed consent should be obtained in human studies and it should be stated in the manuscript.

When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

The authors should describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results. They should define statistical terms, abbreviations, symbols and should specify the statistical software package(s) and versions used.

Results [Findings]

You should present your results in logical sequence in the text, tables, and figures, giving the main or most important findings first. Please, do not repeat all the data in the tables or figures in the text; emphasize or summarize only the most important observations. Provide data on all primary and secondary outcomes identified in the Methods Section. Extra or supplementary materials and technical details can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

You should give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them, if any. You should restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Please, use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample." Separate reporting of data by demographic variables, such as age and sex, facilitate pooling of data for subgroups across studies and should be routine, unless there are compelling reasons not to stratify reporting, which should be explained.

Discussion

It is useful to begin the discussion by briefly summarizing the main findings and explore possible mechanisms or explanations for these findings. Emphasize the new and important aspects of your study and put your findings in the context of the totality of the relevant evidence. State the limitations of your study and explore the implications of your findings for future research and for clinical practice or policy. Do not repeat in detail data or other information given in other parts of the manuscript, such as in the Introduction or the Results [Findings] section.

Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted but label them clearly.

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In-text Citations and References

Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests. Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. On the other hand, extensive lists of references to original work on a topic can use excessive space. Fewer references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently.

Do not use conference abstracts as references: they can be cited in the text, in parentheses, but not as page footnotes. References to papers accepted but not yet published should be designated as "in press". Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source.

Laws (e.g., penal code), statutes and regulations are not scientific writings. In addition to being published on the official gazette, since it is published on various internet sites, a reference number should not be given to laws, statutes and regulations. If it is to be cited within the text, the law could be cited by specifying the number of the law, the date and number of publications in the official gazette (e.g., A Review of Article 5 of the Turkish Criminal Penal Code No. 5237). They should not be numbered within the text, or in the reference list.

To minimize citation errors, references can be verified using either an electronic bibliographic source, such as PubMed, or print copies from original sources. References should be numbered consecutively in the order in which they are first mentioned in the text. Roman numerals should be avoided. Identify references in text, tables, and legends by Arabic numerals (1, 2, 3 … 9, 0) in parentheses. References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals).

If you refer to a work more than once, use the first number also for the second and following references. References to more than one source in the same phrase may be entered like this: (2-4), i.e., references 2 through 4 in the reference list, and (2-4, 8), i.e. the references 2 through 4, plus reference no 8 in the list of references.

Sample for in-text citation:

In a clinical research in healthy individuals, Ellis (25) has studied the sciatic nerve excursion using ultrasound technique.

Wright and Ellis (10) has investigated the excursion of nerves around the elbow joint.

In another and similar cadaveric study by Wright et al (13), the radial nerve median excursion values were 4.1, 8.8, and 0.2, 0.1 mm with motions of shoulder, elbow, wrist and fingers respectively.

Suicide is a major public health problem and globally the second leading cause of death among young adults (1). Studies focusing on how mental health risk factors impact on youth suicidal behaviors suggest that psychopathological symptoms are associated with suicidal behavior (3,4). Adverse effects of H2S on human health vary from local irritation to immediate death depending on the form, concentration, duration and route of exposure (9, 13-15).

Reference Style

The Vancouver system, also known as Vancouver reference style or the author–number system, is a citation style that uses numbers within the text that refer to numbered entries in the reference list. Vancouver style is used by MEDLINE and PubMed. The names "Vancouver system" or "Vancouver style" have existed since 1978. The latest version of the latter is Citing Medicine, per the References > Style and Format section of the ICMJE Recommendations. In 1978, a committee of editors from various medical journals, the International Committee of Medical Journal Editors (ICMJE), met in Vancouver, BC, Canada to agree to a unified set of requirements for the articles of such journals. This meeting led to the establishment of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (URMs). Part of the

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URMs is the reference style, for which the ICMJE selected the long-established author–number principle.

Since the early to mid-2000s, the United States National Library of Medicine (which runs MEDLINE and PubMed) has hosted the ICMJE's "Sample References" pages. Around 2007, the NLM created Citing Medicine, its style guide for citation style, as a new home for the style's details. The ICMJE Recommendations now point to Citing Medicine as the home for the formatting details of Vancouver style.

Scientific Reports in Medicine, since the first day of its publication uses the PubMed/NLM reference style. Thus, references should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals: Samples of Formatted References for Authors of Journal Articles web page and detailed in the NLM's Citing Medicine, 2nd edition.

According to the Vancouver rules, you can only refer to the literature you have read yourself. If you find anything interesting in a text where it is referred to another text, you must read and refer to the original.

Reference List

The reference list should be ordered numerically in the order in which the references appear in the text.

The journal's name may be abbreviated, according to the abbreviation rules for journal titles. Records retrieved from a search for the full journal title in the National Library of Medicine's search page include the abbreviated title.

Authors' names should be given as surname followed by initials. There should be a space between surname and initials. A maximum of two initials are allowed for each author, they should be entered without spaces or punctuation. Different authors should be separated by a space and a comma. A period (.) should follow the last author's name. If six or more authors, list the first six authors followed by et al.

Only capital letter of the first word of the title, proper nouns, proper adjectives, acronyms, and initialisms should be capitalized.

The most reliable method for calculating the impact factor of our journal and number of citations of articles published in our journal or calculating the number of times your own article is cited in a healthy way, is to add DOIs to the references section. In order to give the DOIs to the articles published in Scientific Reports in Medicine, the CrossRef membership application has been completed and all the research articles, case reports, and reviews are being assigned DOIs. For this reason, DOIs need to be added to the References section if available for those references. We hope that the Simple Text Query Form will be helpful in referencing articles published in our journal. With the help of the Simple Text Query Form web page, which has a link in the full-text template, DOI records need to be added to the sources.

https://apps.crossref.org/SimpleTextQuery

Note: Please, do not insert Pubmed ID (PMID) or Pubmed Central ID (PMCID) records to the reference list since they are useless in determining the citation counts.

We place great importance to the addition of DOIs to the references.

Sample for Journal Article without DOI

Dokgöz H, Kar H, Bilgin NG, Toros F. Forensic Approach to Teenage Mothers Concept: 3 Case Reports. Turkiye Klinikleri J Foren Med 2008;5(2):80-4

Kaufman DM, Mann KV, Miujtjens AM, Van der Vleuten CP. A comparison of standard setting procedures for an OSCE in undergraduate medical education. Academic Medicine 2000;75:267–71.

Sample for Journal Article with DOI

Koçak U, Alpaslan AH, Yağan M, Özer E. Suicide by Homemade Hydrogen Sulfide in Turkey a Case Report. Bull Leg Med. 2016;21(3):189-192. https://doi.org/10.17986/blm.2016323754

Article not in English

Kar H, Dokgöz H, Gamsız Bilgin N, Albayrak B, Kaya Tİ. Lazer Epilasyona Bağlı Cilt Lezyonlarının Malpraktis Açısından Değerlendirilmesi. Bull Leg Med. 2016;21(3):153-158. https://doi.org/10.17986/blm.2016323748

Books and Other Monographs

Personal author(s)

Scientific Reports in Medicine

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

Editor(s), compiler(s) as author

Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors. Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.

Author(s) and editor(s)

Breedlove GK, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services; 2001.

Chapter in a book

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113

Emmerson BT. Gout and renal disease. In: Massry SG, Glassock RJ (Editors). Textbook of Nephrology 1. Baskı, Baltimore: Williams and Wilkins; 1989. p. 756–760.

Conference proceedings

Harnden P, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.

Article published on the Internet ahead of the print version:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Part of a homepage/Web site [Edited 28 Dec 2016]

American Medical Association [Internet]. Chicago: The Association; c1995-2016 [cited 2016 Dec 27]. Office of International Medicine; [about 2 screens]. Available from: https://www.ama-assn.org/about/office-international-medicine

Thesis

Skrtic L. Hydrogen sulfide, oil and gas, and people's health [Master's of Science Thesis]. Berkeley, CA: University of California; 2006.

Weisbaum LD. Human sexuality of children and adolescents: a comprehensive training guide for social work professionals [master's thesis]. Long Beach (CA): California State University; 2005. 200 p.

For the reference types not listed here, please visit Samples of Formatted References for Authors of Journal Articles available at Medline Web site (https://www.nlm.nih.gov/bsd/uniform_requirements.html).

Tables

Tables capture information concisely and display it efficiently; they also provide information at any desired level of detail and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text.

It would be appropriate to place the tables at the end of the main text. Number tables consecutively in the order of their first citation in the text and supply a title for each. Titles in tables should be short but self-explanatory, containing information that allows readers to understand the table's content without having to go back to the text. Be sure that each table is cited in the text. Give each column a short or an abbreviated heading. In the tables, case counts (n) and percentages (%) should be specified in separate columns, not in the same cell.

Authors should place explanatory matter in footnotes, not in the heading. Explain all nonstandard abbreviations in footnotes and use symbols to explain information if needed. Symbols may be as alphabet letters or such symbols as *, p t> T §). Please, identify statistical measures of variations, such as standard deviation and standard error of the mean.

Illustrations (Figures)

The lexical meaning of figure constitutes a number symbol (numeral, digit), a written or printed character, a diagram or pictorial illustration of textual matter, arithmetical calculation or digits representing an amount when plural. While definition of picture includes a design or representation made by various means (as painting, drawing, or photography), illustration means a picture or diagram that helps make something clear or attractive. Although these terms bear distinctive meanings, they are too often used interchangeably. Thus, we meant them in the same way without distinction.

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Digital images

The 300 DPI Story

In the ancient times when digital cameras have not been invented, the photos taken by analogue cameras were used to be printed on photo papers. In order to transfer these photos to the digital environment, they had to be scanned by optical devices called scanners. On the same dates, desktop publishing and printing technology was far beyond the digital photography, and many years had passed since the invention of laser printing technology. Here, several technical terms should be explained to make the concept clearer. DPI is used to describe the resolution number of dots per inch in a digital print and the printing resolution of a hard copy print dot gain, which is the increase in the size of the halftone dots during printing. A dot matrix printer, for example, applies ink via tiny rods striking an ink ribbon, and has a relatively low resolution, typically in the range of 60 to 90 DPI (420 to 280 μm). An inkjet printer sprays ink through tiny nozzles and is typically capable of 300–720 DPI. A laser printer applies toner through a controlled electrostatic charge and may be in the range of 600 to 2,400 DPI. Along with the cheaper memory chips, 1200 dpi printers have been widely available in the consumer market since 2008. Monitors do not have dots but do have pixels. The closely related concept for monitors and images is pixels per inch or PPI. Old CRT type video displays were almost universally rated in dot pitch, which refers to the spacing between the subpixel red, green and blue dots which made up the pixels themselves. The DP measurement of a printer often needs to be considerably higher than the pixels per inch (PPI) measurement of a video display in order to produce similar-quality output. This dithered printing process could require a region of four to six dots (measured across each side) in order to faithfully reproduce the color in a single pixel. An image that is 100 pixels wide may need to be 400 to 600 dots in width in the printed output; if a 100×100-pixel image is to be printed in a one-inch square; the printer must be capable of 400 to 600 dots per inch to reproduce the image. The dpi of early model laser printers was 300 to 360, thus scanning images at 300 DPI was a common practice at that time.

In printing, DPI (dots per inch) refers to the output resolution of a printer or imagesetter, and PPI (pixels per inch) refers to the input resolution of a photograph or image. DPI refers to the physical dot density of an image when it is reproduced as a real physical entity, for example printed onto paper. A digitally stored image has no inherent physical dimensions, measured in inches or centimeters. Some digital file formats record a DPI value, or more commonly a PPI (pixels per inch) value, which is to be used when printing the image. This number lets the printer or software know the intended size of the image, or in the case of scanned images, the size of the original scanned object. For example, a bitmap image may measure 1,000 × 1,000 pixels, a resolution of 1 megapixel. If it is labeled as 250 PPI, that is an instruction to the printer to print it at a size of 4 × 4 inches. Changing the PPI to 100 in an image editing program would tell the printer to print it at a size of 10×10 inches. However, changing the PPI value would not change the size of the image in pixels which would still be 1,000 × 1,000. An image may also be resampled to change the number of pixels and therefore the size or resolution of the image, but this is quite different from simply setting a new PPI for the file.

Therefore, an image that is 2048 pixels in width and 1536 pixels in height has a total of 2048×1536 = 3,145,728 pixels or 3.1 megapixels. One could refer to it as 2048 by 1536 or a 3.1-megapixel image. Or, you can think of it as a very low-quality image (72 ppi) if printed at about 28.5 inches wide, or a very good quality (300 ppi) image if printed at about 7 inches wide.

Since the 1980s, the Microsoft Windows operating system has set the default display "DPI" to 96 PPI, while Apple/Macintosh computers have used a default of 72 PPI. The choice of 72 PPI by Macintosh for their displays arose from the convenient fact that the official 72 points per inch mirrored the 72 pixels per inch that appeared on their display screens. (Points are a physical unit of measure in typography, dating from the days of printing presses, where 1 point by the modern definition is 1/72 of the international inch (25.4 mm), which therefore makes 1 point approximately 0.0139 in or 352.8 μm). Thus, the 72 pixels per inch seen on the display had exactly the same physical dimensions as the 72 points per inch later seen

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on a printout, with 1 pt in printed text equal to 1 px on the display screen. As it is, the Macintosh 128K featured a screen measuring 512 pixels in width by 342 pixels in height, and this corresponded to the width of standard office paper (512 px ÷ 72 px/in ≈ 7.1 in, with a 0.7 in margin down each side when assuming 8.5 in × 11 in North American paper size (in Europe, it's 21 cm x 30 cm - called "A4")).

In computing, an image scanner—often abbreviated to just scanner, is a device that optically scans images, printed text, handwriting or an object and converts it to a digital image. Although the history of digital cameras dates back to the 1970s, they have become widely used in the 2000s. While the resolution of the first digital camera invented by Kodak was as low as 100 by 100 pixels (0.01 megapixels), the first commercially available digital camera, Fujix DS-1P had a resolution of 0.4 megapixels. On the other hand, modern scanners are considered the successors of early telephotography and fax input devices. The pantelegraph was an early form of facsimile machine transmitting over normal telegraph lines developed by Giovanni Caselli, used commercially in the 1860s, that was the first such device to enter practical service. The history of the first image scanner developed for use with a computer goes back to 1957. Color scanners typically read RGB (red-green-blue color) data from the array. This data is then processed with some proprietary algorithm to correct for different exposure conditions and sent to the computer via the device's input/output interface. Color depth varies depending on the scanning array characteristics but is usually at least 24 bits. High quality models have 36-48 bits of color depth. Another qualifying parameter for a scanner is its optical resolution, measured in pixels per inch (ppi), sometimes more accurately referred to as samples per inch (spi).

Images in web pages, video, and slide shows can be as low as 72 PPI for a static image or 150 PPI if we are going to focus in on the image. For printing, the DPI needs to be larger, with images scanned in at least 300 DPI. The DPI standard for and images to be printed within journals and books is 300 DPI and for museum exhibits, it's 600 DPI.

The most important factors determining image quality of digital images can be considered as pixel dimensions and color depth. Increasing the dpi value of an image by resampling in Photo Editors (e.g., Adobe Photoshop) has no improving effect on its quality, but it lets us to determine target printing size.

For vector images, there is no equivalent of resampling an image when it is resized, and there is no PPI in the file because it is resolution independent (prints equally well at all sizes). However, there is still a target printing size. Some image formats, such as Photoshop format, can contain both bitmap and vector data in the same file. Adjusting the PPI in a Photoshop file will change the intended printing size of the bitmap portion of the data and also change the intended printing size of the vector data to match. This way the vector and bitmap data maintain a consistent size relationship when the target printing size is changed. Text stored as outline fonts in bitmap image formats is handled in the same way. Other formats, such as PDF, are primarily vector formats which can contain images, potentially at a mixture of resolutions. In these formats the target PPI of the bitmaps is adjusted to match when the target print size of the file is changed. This is the converse of how it works in a primarily bitmap format like Photoshop but has exactly the same result of maintaining the relationship between the vector and bitmap portions of the data.

Long story short, it is not technically possible to talk about DPI value for images that were taken by digital cameras or any type of digital images that were transferred to the computer's storage media. The DPI value stored within exif information of images is just a virtual value just to guide the photo editing software and the graphic artist to determine the target printing size of that image.

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Each vector graphic software has its own built-in settings and may have been preset at 72 dpi. So, the document should be created enough big to obtain the image in the desired dimensions. The vector graphics should be exported to a rasterized image format and inserted such as JPEG or TIFF files.

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As the journal Scientific Reports in Medicine (SRINMED), we are excited to share with you the excitement of continuing our publication journey and we are happy to share it with you, our valued science readers. I would like to thank all the authors who contributed to our 5th issue.

Editor-in-Chief

Assoc. Prof. Dr. Burak METE

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Ceren Kanat Şahin[1], Tuğba Demirbaş Üstün [2] , Ece Şenkaya[3], İlker Kanlı[4], Mehmet Ali Küçüközkan[5], Lütfullah Yerlikaya[6], Mavisu Kandemir[7], Fadime Yapıcı[8], Sakhr Al Dhelaa[9], Mert Tekemen[10]

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Abstract: Objective: Family planning plays a crucial role in public health by enabling individuals to control their reproductive choices in a responsible and informed manner. However, migrant populations often face barriers to accessing these services, leading to increased rates of unintended pregnancies and reproductive health complications. This study aims to assess the knowledge, attitudes, and behaviors regarding family planning among migrants living in Adana, Turkey, compared to the local population.

Methods: This cross-sectional study was conducted in January 2025 at Doğankent Family Health Center and Doğankent Migrant Health Center. The study population included individuals aged 15-49 who voluntarily participated. A structured questionnaire was administered through face-to-face interviews to collect sociodemographic data, knowledge levels, and usage patterns of modern family planning methods. The sample size was determined as 220 participants with 95% power and a 5% confidence interval; ultimately, data from 245 individuals were analyzed. Statistical analyses were performed using SPSS 20 software, employing the Kolmogorov-Smirnov test for normality assessment, parametric (t-test), non-parametric (Mann-Whitney U test), and categorical comparisons (chi-square test). A p-value of <0.05 was considered statistically significant.

Results: Of the 245 participants, 143 (58%) were locals and 102 (42%) were migrants. Although knowledge of modern family planning methods was similar in both groups, actual use of modern methods was significantly lower among migrants (38.6% vs. 51.4%; p = 0.049). Barriers to modern contraceptive use included lack of partner consent, limited accessibility and economic constraints.

Keywords: Contraception, Migrants, Reproductive Health

[1]Tarsus District Health Directorate, Mersin, Turkey
ORCID iD:0000-0003-4858-9275

[2]Research Assistant Phd. Çukurova University Faculty Of Medicine Department Of Public Health Adana,Turkey
ORCID iD: 0009-0007-0953-0031

[3]Medical Intern, Çukurova University Faculty of Medicine, Adana,Turkey
ORCID iD: 0009-0007-2961-5067

[4]Medical Intern, Çukurova University Faculty of Medicine ,Adana,Turkey
ORCID iD: 0000-0001-6792-6455

[5]Medical Intern, Çukurova University Faculty of Medicine, Adana, Turkey
ORCID iD: 0009-0004-9328-7158

[6]Medical Intern, Çukurova University Faculty of Medicine, Adana, Turkey
ORCID iD: 0009-0007-3966-003X

[7]Medical Intern, Çukurova University Faculty of Medicine, Adana, Turkey
ORCID iD: 0009-0005-8960-3629

[8]Medical Intern, Çukurova University Faculty of Medicine, Adana, Turkey
ORCID iD: 0009-0001-8764-3599

[9]Medical Intern, Çukurova University Faculty of Medicine, Adana, Turkey
ORCID iD: 009-0004-6364-1945

[10]Medical Intern, Çukurova University Faculty of Medicine, Adana, Turkey
ORCID iD: 0009-0004-3408-7674

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INTRODUCTION

Family planning is a process that allows individuals to consciously and responsibly control the timing, number, and spacing of their children. According to the World Health Organization (WHO), family planning not only aims to prevent pregnancies but also seeks to protect the health of mothers and children and support individuals' reproductive rights (1). Family planning services help individuals avoid unwanted pregnancies, prevent sexually transmitted infections, and reduce reproductive health risks. While improving individuals' quality of life, family planning also positively impacts public health.

Today, modern family planning methods are preferred over traditional methods due to their reliability and effectiveness. Modern methods include oral contraceptives, condoms, intrauterine devices (IUDs), sterilization, and hormonal injections (2).

Modern family planning services in Turkey began with the adoption of the Population Planning Law in 1965 and have since become an integral part of public health programs (3). According to the 2018 Turkey Demographic and Health Survey (TDHS) conducted by the Hacettepe University Institute of Population Studies, 47.4% of women of reproductive age use a modern family planning method. However, this rate varies between rural and urban areas, being lower in rural regions (4). Additionally, education level, socioeconomic status, and access to healthcare services are among the primary factors influencing the use of modern methods.

It has been reported that migrants do not benefit sufficiently from family planning services, may experience unwanted pregnancies, have incomplete pregnancy check-ups, and face higher rates of birth complications, maternal and perinatal mortality risks, and despite these challenges, maintain high fertility rates (5).

The aim of our study is to determine the knowledge, attitudes, and behaviors of migrants living in Adana regarding family planning in comparison to the local population.

MATERIALS AND METHODS

This cross-sectional study was conducted in January 2025 at the Doğankent Family Health Center and the Doğankent Migrant Health Center among individuals aged 15-49. Approval for the study was obtained from the Çukurova University Ethics Committee.

The sample size was determined as 220 individuals based on a reference sample size analysis with 95% power and a 5% confidence interval (r=0.5). A total of 245 participants were reached using the convenience sampling method. Face-to-face interviews were conducted with voluntary participants using a questionnaire.

The questionnaire included socio-demographic information (age, number of children, employment status, income level, health insurance, marital status) and questions assessing knowledge about family planning methods, receipt of family planning information, use of modern family planning methods, reasons for non-use, type of method used, and factors influencing method selection.

Statistical analysis

Data were analyzed using the SPSS 20 software. The Kolmogorov-Smirnov test was used to assess normal distribution. Parametric tests (t-tests) were applied to normally distributed data, non-parametric tests (Mann-Whitney U test) were used for non-normally distributed data, and chi-square tests were used for categorical data comparisons. A p-value of <0.05 was considered statistically significant.

RESULTS

Of the 245 participants included in the study, 143 (58%) were from the local population, while 102 (42%) were migrants. The average age of the local population was statistically significantly higher than that of the migrant group ($p = 0.001$). The migrant group had a higher number of children ($p = 0.007$). In terms of education level, the migrant group had a lower level of education, with a higher proportion of primary school graduates and illiterate individuals

(p < 0.001). Regarding employment, most migrant women were housewives, and their employment rate was lower (p < 0.001). Income levels showed that most migrant women earned at or below the minimum wage (p < 0.001). Moreover, while the rate of having health insurance was significantly high among the local population (82.4%), it was very low among migrants (2.9%) (p < 0.001).

Table 1. Sociodemographic characteristics by groups

	Median(min-max) or n(%)		
Characteristics	**Local Population**	**Migrant**	**p**
Age	32(16-65)	27(16-58)	**0.001**
Number of Children	2(0-7)	3(0-6)	**0.007**
Education			
University	36(25.5)	1(1.0)	**<0.001**
High school	32(22.7)	7(6.9)	
Secondary school	27(19.1)	34(33.3)	
Primary school	30(21.3)	51(50.0)	
Illiterate	16(11.3)	9(8.8)	
Occupation			
Housewife	88(63.3)	89(87.3)	**<0.001**
Worker	22(15.8)	12(11.8)	
Civil servant	27(19.4)	1(1.0)	
Retired	2(1.4)	0(0.0)	
Employment status			
Employed	51(35.9)	16(15.7)	**<0.001**
Unemployed	91(64.1)	86(84.3)	
Household income (m.w.=29.516 TL)			
Below minimum wage	19(13.5)	19(19.0)	**<0.001**
Minimum wage	58(41.1)	79(79.0)	
More than twice the minimum wage	64(45.4)	2(2.0)	
Health insurance			
Available	117(82.4)	3(2.9)	**<0.001**
Not Available	25(17.6)	99(97.1)	
Marital status			
Married	110(77.5)	95(95.0)	**0.001**
Single	26(18.3)	5(5.0)	
Widowed/Divorced	6(4.2)	0(0.0)	

There was a statistically significant difference between the migrant and local groups in terms of the desire to have children and pregnancy status within the last two years (p=0.047). The proportion of individuals receiving information on family planning methods at Family Health Centers was significantly higher among migrants (p < 0.001). However, the rate of using modern family planning methods was lower among migrants than among the local population (p=0.049). The most commonly preferred modern method among migrants was condom use.

DISCUSSION

TO is an autoimmune disease affecting the thyroid gland and eye (4). Mechanical and inflammatory factors play a significant role in the ocular findings of TO and can change ocular, corneal biomechanical and densitometric properties (5). Reduced tear production and rubbing of eyes, common in Graves' disease, is a known precipitant of keratoconus (KC). Our study showed some differences in corneal biomechanical properties among the patients with TO disease. By using Pentacam all the patients were evaluated and the results of this analysis demonstrate the haziness score at three layers of corneal depth: the anterior layer, comprising 120 μm of anterior cornea; the posterior layer, comprising 60 μm of the extreme posterior cornea; and the central layer, located between the anterior and posterior layers. A total densitometry score is also reported that represents the volume between the epithelium and endothelium. Eventhough there are not enough studies related with the effects of TO on corneal densitomery, we found out that there were significant differences in anterior and posterior layers of 2-6 mm zone (p<0,040, p<0,010), all layers of 6-10 mm zone (p<0,008, p<0,002, p<0,002, p<0,003) and in all layers of overall corneal thickness (p<0,008, p<0,004, p<0,002, p<0,007). During the second month of evaluation, there were significant differences in posterior layers of 0-2mm and 2-6mm zones (p<0,045, p<0,034), and in the central layers of 2-6mm zone and overall corneal thickness (p<0,037, p<0,041). In the last month of evaluation only in the anterior layer of total corneal thickness a significant difference is seen (p<0,03). We can say that every stage of TO has effect on corneal densitometry and the most affected one is the anterior layer which is supposed to lead to the thinning of epithelial layer. Previous studies have analyzed mostly corneal densitometries of keratoconus, primary congenital glaucoma and outcomes after keratoplastic surgeries. Lopes et al.[5] found out a higher densitometry in all layers of the central cornea (p<0.001). The difference was marked in all layers of 0-2mm and 2-6mm zones and these values were detected in different stages of KC (5). Monitoring the cornea in patients with TO using Pentacam may help to show the presence of subclinical inflammation and regulate the follow-up and treatment protocols. For this reason larger sample sizes and prospective design studies are needed to reach more conclusive results.

It is known that increased expression of inflammatory mediators in tears of GO patients suggests that the lacrimal glands could be a target for immune responses and this may play role in the pathogenesis of tear film and ocular surface stability (6). The pathophysiologic alterations of active TO could result in an increase in orbital soft tissue volume, which pushes the globe anteriorly, leading to raised retrobulbar pressure and progression of proptosis (7). In our study, hertel exophthalmometry measurements increased during the severity of TO and significant differences were seen in the 1st month in mild and severe TO patients (p<0,041) and 3rd month especially in patients with mild-moderate (p<0.025) and mild-severe TO (p<0,020). Same results were found in the study of Tran et al.[8], where at initial presentations 41% of their patients demonstrated asymmetric proptosis (8). Upon reaching the stable phase, asymmetric proptosis persisted in only 22% of patients. A decline in the rate asymmetric proptosis was greatest within the first 3 months of the active phase (8). During the third month the retinal nerve fiber layer values were significantly thinner in patients with moderate-severe TO (p<0,029). Luo et al.[9], no statistically significant differences were found between the mild thyroid-associated opthalmopathy group and the control group in nerve fiber layers of patients (9). In the moderate-to-severe thyroid-associated opthalmopathy group, temporal and nasal peripapillary nerve fiber layer thicknesses were lower compared to the control group ($p = 0.041$, $p = 0.012$). The thinning of RNFL might be a strong suggestion for closer vision follow-up and earlier decompression surgery.

Almost 50% of patients with TO symptoms are mild (10). If the diagnosis couldn't be performed at the active phase, some cases might have severe

Table 2. Methods offered by the family and the level of knowledge among immigrants compared to local people			
	Median(min-max) or n(%)		
Characteristics	**Local population**	**Migrant**	**p**
Desire to have children			
Yes	48(35.6)	48(48.5)	0.047
No	87(64.4)	51(51.5)	
Pregnancy status in the last 2 years			
Yes	45(31.9)	56(56.0)	<0.001
No	96(68.1)	44(44.0)	
Knowledge about family planning method			
Yes	106(75.7)	90(90.0)	0.005
No	34(24.3)	10(10.0)	
Knowledge of modern family planning methods (Ex. Birth control pills, IUD, Condom, Sterilization etc.)			
Yes	114(80.9)	87(87.0)	0.206
No	27(19.1)	13(13.0)	
Status of providing information about family planning in FHC			
Yes	94(66.7)	88(88.0)	<0.001
No	47(33.3)	12(12.0)	
Current use of family planning methods			
Yes	72(51.4)	39(38.6)	0.049
No	68(48.6)	62(61.4)	
If no, why?			
Pregnant	2(3.8)	22(45.8)	<0.001
Not neccessary	18(34.0)	12(25.0)	
Single	15(28.3)	3(6.3)	
I want to have children	11(20.8)	1(2.1)	
I shouldn't use it	0(0.0)	4(8.3)	
I don't want to use	5(9.4)	6(12.5)	
I am not informed	1(1.9)	0(0.0)	
Expensive	1(1.9)	0(0.0)	
Which is used as a modern family planning method?			
Oral Contraceptive Pills	19(21.6)	6(12.5)	<0.001
Intrauterine Device	16(18.2)	3(6.3)	
Condom	30(34.1)	37(77.1)	
Hormonal Injection	1(1.1)	1(2.1)	
Implant	1(1.1)	0(0.0)	
Tubal Ligation	10(11.4)	0(0.0)	
Withdrawal Method	4(4.5)	0(0.0)	
Not Using	7(8.0)	1(2.1)	
Has a modern family planning method been used before?			
Yes	79(56.4)	73(71.6)	0.016
No	61(43.6)	29(28.4)	

sight-A statistically significant difference was found between the local population and migrants in terms of receiving family planning counseling services and healthcare providers ($p < 0.001$). Among migrant participants, 82.4% reported receiving family planning counseling services, compared to 61% of the local population. The rate of obtaining information about families in ASM is higher than that of the immigrant class (88%), but examination services are mostly provided by officials and midwives rather than doctors. When the most important factor in choosing a modern family planning method was questioned, a statistically significant difference was observed between the two groups (p=0,015). The most common reason for method preference among migrants was ease of use (58%), whereas 37.2% of the local population emphasized effectiveness as the most crucial factor. Among the reasons for not using modern methods, the response "my spouse does not approve" was prominent in the migrant group. A significant difference was also found between the groups regarding difficulties in accessing family planning methods ($p < 0.001$). While 36% of migrants reported experiencing difficulty in accessing family planning methods, this rate was 12.4% among the local population.

Table 3. Knowledge, Attitudes, and Behaviors Regarding Family Planning Methods Among Migrants and the Local Population

	Median (min-max) or n (%)		
Characteristics	**Local population**	**Migrant**	**p**
Received family planning counseling from any healthcare institution (e.g., FHC, hospital, etc.)			
Yes	86 (61.0)	84 (82.4)	<0.001
No	55 (39.0)	18 (17.6)	
If counseling was received, which healthcare professional provided it?			
Doctor	57 (58.8)	5 (5.7)	<0.001
Nurse/Midwife	38 (39.2)	82 (93.2)	
Did not receive counseling	2 (2.1)	1 (1.1)	
Did the received counseling service provide sufficient information on modern family planning methods?			
Yes	84 (74.3)	74 (81.3)	0.236
No	29 (25.7)	17 (18.7)	
Did the counseling service influence your decision to use a modern family planning method?			
Yes	63 (57.3)	66 (72.5)	0.025
No	47 (42.7)	25 (27.5)	
How did you decide to use a modern family planning method?			
Healthcare professional's recommendation	14 (23.3)	14 (34.1)	0.104
Based on my own research	13 (21.7)	7 (17.1)	
Family members/Friends' recommendation	7 (11.7)	0 (0.0)	
Together with my spouse/partner	19 (31.7)	15 (36.6)	
Based on previous experiences	4 (6.7)	5 (12.2)	
Not using any method	3 (5.0)	0 (0.0)	
What was the most important factor in choosing a modern family planning method?			

Effectiveness (pregnancy prevention rate)	19 (32.7)	4 (11.8)	0.015
Ease of use	13 (22.4)	20 (58.8)	
Cost/Accessibility	2 (3.4)	3 (8.8)	
Spouse/Partner's preference	11 (19.0)	4 (11.8)	
Healthcare professional's recommendation	3 (5.2)	2 (5.9)	
Fewer side effects	8 (13.8)	1 (2.9)	
Not using any method	2 (3.4)	0 (0.0)	
Reasons for not using modern methods			
Fear of side effects	9 (19.1)	0 (0.0)	0.125
Spouse does not approve	12 (25.5)	8 (50.1)	
Religious reasons	5 (10.6)	2 (12.5)	
Lack of access	3 (6.4)	3 (18.8)	
Single	9 (19.1)	1 (6.3)	
Pregnant	2 (4.3)	1 (6.3)	
Other	7 (14.9)	1 (6.3)	
Who do you discuss family planning with?			
Doctor	20 (26.0)	3 (3.8)	<0.001
Spouse	33 (42.9)	61 (76.3)	
Family members	4 (5.2)	11 (13.8)	
Friends	15 (19.5)	5 (6.3)	
No one	5 (6.5)	0 (0.0)	
Does your spouse support your use of family planning?			
Yes	81 (68.6)	59 (62.1)	0.318
No	37 (31.4)	36 (37.9)	
Do you experience difficulties in accessing family planning methods?			
Yes	16 (12.4)	36 (36.0)	<0.001
No	113 (87.6)	64 (64.0)	
Do you think you need more information about family planning methods?			
Yes	44 (32.1)	48 (48.5)	0.011
No	93 (67.9)	51 (51.5)	
Is the counseling service you received at FHC sufficient?			
Yes	90 (73.2)	75 (76.5)	0.568
No	33 (26.8)	23 (23.5)	
Do you think modern family planning methods are harmful to health?			
Yes	25 (18.7)	15 (14.9)	0.442
No	109 (81.3)	86 (85.1)	
Have you considered receiving family planning services from another healthcare facility?			
Yes	20 (14.8)	24 (24.5)	0.062
No	115 (85.2)	74 (75.5)	

DISCUSSION

The accessibility of family planning services for migrant individuals varies based on their level of integration into the healthcare system, economic conditions, and cultural values. Modern family planning methods are crucial for protecting individuals' health, preventing unwanted pregnancies, and optimizing reproductive health.

The proportion of individuals aware of modern family planning methods was similar between the local population (80.9%) and migrants (87.0%). However, significant differences existed in terms of usage rates: 51.4% of the local population used modern methods compared to only 38.6% of migrants. Family Health Centers serve as important sources of information for modern family planning methods. While 66.7% of the local population received family planning information from these centers, this rate was 88% among migrants. However, this high rate of awareness did not fully translate into the adoption of modern methods. Economic and cultural barriers might be preventing migrant individuals from utilizing these services.

The median number of children among migrants was higher than that among the local population. A higher number of children increases the need for family planning services, and failure to meet this need may lead to health complications. The finding that migrant women have more children at a younger age aligns with international literature. For example, Benova et al. (6) reported that migrant women tend to have children at a younger age and in higher numbers compared to local women. This can be explained by cultural norms and lower education levels within migrant communities. In our study, migrant women were found to have lower education levels, with most being primary school graduates or illiterate. Education level is identified as a key factor in adopting family planning methods (7).

The lower rate of modern family planning method use among migrants is consistent with the literature, which suggests that migrant women tend to prefer traditional methods more (8). The predominance of condom use among migrants is a significant finding, which can be attributed not only to its accessibility and low cost but also to its male-controlled nature, reflecting a male-centered approach to contraception. Among the reasons for not using modern methods, "husband does not approve" was a frequently cited response, highlighting the influence of gender roles on migrant women's decision-making regarding family planning (9).

Globally, the use of modern methods increased from 35% in 1990 to 45% in 2021 (10). This rate varies across countries due to differences in socioeconomic conditions, cultural factors, and healthcare accessibility. The use of modern methods remains lower in low- and middle-income countries, leading to higher rates of unintended pregnancies (11).

Among migrant women in Turkey, family planning knowledge and utilization levels are lower compared to the local population (12). Studies indicate that migrant women face challenges such as language barriers, cultural factors, and economic difficulties in accessing family planning services (13). Limited use of modern contraceptive methods among migrant women is associated with higher rates of unintended pregnancies. This pattern may, in part, be explained by the fact that a considerable number of women are already pregnant at the time of migration, which may delay or reduce the perceived need for contraception.

Limitations of the study

Limitation of this study is that it was conducted in only one Family Health Center and one Migrant Health Center within the province of Adana. Incorporating data from different regions could allow for more comparative and generalizable findings.

CONCLUSION

Our study reveals significant differences in family planning methods and access to healthcare services between the local population and migrant women. While migrant women exhibit high awareness of modern family planning methods, their actual usage rate is lower compared to the local population.

To overcome barriers to accessing modern family planning methods, healthcare services must be redesigned with cultural sensitivity. Family Health Centers should enhance their educational and informational efforts while addressing language barriers and cultural differences. Economic support programs can also improve access to these services.

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Evaluation of the Effect of Virtual Reality Glasses on Preoperative Surgical Anxiety in Adult Patients

Effect of VR on Preoperative Anxiety

Semih Güner[1], Osman Ekinci[2], Çağdaş Baytar[3], Burak Mete[4]

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Abstract: Objective: Patients often experience varying levels of anxiety before surgery. It is essential to assess and address preoperative anxiety for each patient to ensure optimal outcomes. This study aims to evaluate the effectiveness of virtual reality (VR) glasses in reducing preoperative anxiety in patients undergoing laparoscopic cholecystectomy.

Method: This prospective, observational cohort study included 84 patients aged 18–65 scheduled for elective laparoscopic cholecystectomy with an American Society of Anesthesiologists (ASA) physical status of I or II. Participants viewed a 30-minute VR video using a smartphone and VR headset. Oxygen saturation and heart rate were recorded before and after the VR session. Additionally, patients completed the "Anxiety Specific to Surgery Questionnaire" both before and after the VR intervention.

Results: The study included 84 patients undergoing laparoscopic cholecystectomy. The VR intervention significantly reduced preoperative anxiety, as indicated by the questionnaire results ($p < 0.001$), with a moderate effect size. Although heart rate decreased after the VR session, the change was not statistically significant.

Conclusion: The use of VR significantly reduced preoperative anxiety in patients scheduled for laparoscopic cholecystectomy.

Keywords: preoperative anxiety, laparoscopic cholecystectomy, virtual reality

[1]Health Sciences University Haydarpasa Numune Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Türkiye
Email: semihgnr@hotmail.com
ORCID iD: 0009-0007-8694-2056

[2]Health Sciences University Haydarpasa Numune Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Türkiye
Email: droekinci@gmail.com
ORCID iD: 0000-0002-7891-1774

[3]Zonguldak Bülent Ecevit University Medicine Faculty, Department of Anesthesiology and Reanimation, Zonguldak, Türkiye
Email: cagdasbaytar31@gmail.com
ORCID iD: 0000-0001-7872-9676
0000-0002-0780-6176

[4]Çukurova University Medicine Faculty, Department of Public Health, Adana, Türkiye
Email: burakmete2008@gmail.com
ORCID iD: 0000-0002-0780-6176

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INTRODUCTION

Millions of people undergo surgical procedures each year, and this number has been steadily increasing over time (1). To ensure optimal outcomes, patients must be well-prepared for surgery, have their needs addressed, be informed about the process, remain vigilant regarding potential complications, and have their anxiety effectively managed (2). Despite comprehensive preoperative services and preparations, many patients still struggle with surgical anxiety (3).

It is well-documented that a significant proportion of patients experience varying levels of anxiety before surgery. Studies indicate that approximately 60–80% of patients report preoperative anxiety (4-7). Inadequate psychological preparation during this period can impair a patient's ability to cope with stress and lead to a sense of inadequacy or loss of control (8-11). Therefore, it is essential to assess and manage preoperative anxiety for each patient individually.

Pharmacological methods are commonly used to reduce anxiety during the perioperative period. However, these medications may delay postoperative recovery due to their lingering effects on the central nervous system. As a result, non-pharmacological interventions—such as music therapy, hypnosis, acupuncture, progressive muscle relaxation, and virtual reality (VR)—are gaining popularity for managing perioperative anxiety (6,12).

Virtual reality technology allows patients to view and hear immersive digital content through a headset, which blocks out their surroundings and helps reduce environmental stressors. These headsets typically deliver calming audio—such as music or natural sounds—while eliminating ambient hospital noise. By simulating relaxing virtual environments, VR technology enables patients to become absorbed in an interactive world, providing a powerful distraction from anxiety-inducing stimuli. Several studies have shown that VR can effectively reduce both preoperative and postoperative anxiety and pain through this distraction mechanism (13-18).

This study aims to evaluate the effectiveness of VR glasses in reducing preoperative anxiety in adult patients undergoing laparoscopic cholecystectomy.

METHOD

This study was conducted between 2019 and 2020 at the University of Health Sciences Haydarpaşa Numune Training And Research Hospital, following approval from the institutional ethics committee (HNHAH-KAEK 2019/155).

The study included voluntary patients aged 18 to 65 years, scheduled to undergo laparoscopic cholecystectomy under general anesthesia, with no additional systemic diseases and classified as ASA physical status I or II.

Exclusion criteria included age under 18 or over 65, a history of congestive heart failure, chronic kidney or liver disease, adrenal insufficiency, hormonal disorders, diabetes, chronic alcohol or substance abuse, a Glasgow Coma Scale score below 15, cerebrovascular disease, psychiatric or cognitive impairment, and cardiopulmonary resuscitation within the past year.

A total of 84 patients were visited in their hospital rooms 24 hours before surgery, provided with detailed information about the study, and included after obtaining written informed consent.

Demographic and clinical data were collected using a questionnaire that included variables such as age, sex, educational level, financial status, and physical activity level.

On the day of surgery, patients were taken to the preoperative holding area, where the procedure was re-explained. Baseline oxygen saturation (SpO2) and heart rate were recorded using a fingertip pulse oximeter.

Preoperative anxiety levels were assessed using the "Anxiety Specific to Surgery Questionnaire," a 10-item Likert-type scale developed in 2003 (Table 1) (19). Each item is rated from 1 (strongly disagree) to 5 (strongly agree), except for item 8, which is reverse-scored. Total scores range from 10 to 50, with higher scores indicating greater anxiety regarding pain, the possibility of death, and postoperative complications (19).

Table 1. Anxiety Specific to Surgery Questionnaire

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1. I often think about the possibility of death.	1	2	3	4	5
2. I worry that something might happen to me and my family and children would be left behind.	1	2	3	4	5
3. I fear not waking up after being put to sleep for the surgery.	1	2	3	4	5
4. I think I might die due to bleeding or another complication during the operation.	1	2	3	4	5
5. I believe I will not fully recover due to postoperative wound infection or another issue.	1	2	3	4	5
6. I fear being unable to walk or take care of myself as before after the surgery.	1	2	3	4	5
7. I think I will experience severe pain after the surgery.	1	2	3	4	5
8. I believe all pain and problems will be resolved after the surgery.	1	2	3	4	5
9. I am afraid of becoming disabled.	1	2	3	4	5
10. I think I will feel pain during the surgery.	1	2	3	4	5

Patients were informed that they would watch a 30-minute video designed to provide a visual and auditory experience. They were told that the anxiety scale would be re-administered after the video.

Patients were placed in a comfortable position, and the VR headset was adjusted for optimal visual and auditory alignment. After ensuring patient comfort and obtaining verbal consent, the video session began. Upon completion, the headset was removed, and SpO2 and heart rate were measured again. The anxiety questionnaire was re-administered.

All patients then underwent surgery under standardized general anesthesia protocols. Intraoperative heart rate and SpO2 monitoring were continued in all cases.

The VR headset used in the study was "VRBOX." The video content consisted of 30 minutes of nature-themed visuals accompanied by relaxing zen music, providing a 360-degree immersive experience. The video was sourced from a publicly available online platform (https://www.youtube.com/watch?v=xskH6VEWV28).

Statistical analysis

Before starting the study, the sample size analysis was performed using a 95% confidence interval and 80% power as reference (group 1: 39.1±4.7, group 2: 34.3±5.7) (20) and found that the minimum sample size to be achieved was 38.

Data were analyzed using the SPSS version 22.0 statistical software. The Kolmogorov-Smirnov test was employed to assess the normality of data distribution.

Qualitative variables were expressed as frequencies and percentages, while quantitative variables were reported as mean, standard deviation, and median values.

For comparisons of non-normally distributed data, the Mann-Whitney U test and Wilcoxon signed-rank test were utilized. Effect sizes were calculated with "effect size calculator". $P<0.05$ was considered significant.

RESULTS

A total of 84 patients undergoing laparoscopic cholecystectomy were included in the study. The mean age was 42.1±9.3 years (range: 24–66). Among the participants, 61.9% were female and 38.1% were male. Additionally, 58.3% were over the age of 40, 41.7% were university graduates, and 54.8% reported earning a minimum wage or less. Regarding ASA classification, 66.7% of patients were ASA I, and 33.3% were ASA II. Based on body mass index (BMI), 96.4% of patients were within the 18–29 range, while 3.6% had a BMI ≥30.

There was a decrease of 1.036 beats per minute in heart rate after the VR intervention, although this reduction was not statistically significant. The mean anxiety scores and their changes before and after VR application are shown in Table 2.

Table 2. Anxiety scores and changes before and after VR

	Anxiety Scores				
	Mean	**SD**	**Median**	**Effect Size (d)**	**p**
Before VR	**33.6**	**4.3**	**34.0**	**0.68**	**<0,001**
After VR	**30.9**	**3.6**	**30.0**		

SD: standard deviation, **VR:** Virtual reality

Analysis of pre- and post-intervention mean anxiety scores revealed that VR significantly reduced anxiety ($p<0.001$), with a moderate effect size ($d = 0.68$).

Female patients demonstrated significantly higher preoperative anxiety levels compared to males, both before and after VR exposure. Nevertheless, VR significantly reduced preoperative anxiety in both sexes, with moderate effect sizes observed in each group (Table 3).

Table 3. Anxiety scores according to depending on sex

Sex		**Before VR**	**After VR**	**p**	**Effect Size**
Female	Mean	34,94	31,83		
	SD	4,30	3,62	**<0,001**	0.78
	Median	36,00	32,00		
Male	Mean	31,41	29,41		
	SD	3,39	3,29	**<0.001**	0.59
	Median	31,50	30,00		
	p	**<0.001**	**0.004**		

SD: standard deviation, **VR:** Virtual reality

No statistically significant differences in preoperative anxiety scores were found based on educational background. Regardless of educational status, VR application significantly reduced preoperative anxiety scores. The intervention showed a moderate effect size in the non-university graduate group and a large effect size in the university graduate group (Table 4).

Table 4. Anxiety scores according to depending on educational background					
Educational Background		**Before VR**	**After VR**	**p**	**Effect Size**
Non-University Graduate	Mean	33,33	30,78		
	SD	4,53	3,91	**<0.001**	0.60
	Median	34,00	30,00		
University Graduate	Mean	33,97	31,09		
	SD	4,04	3,37	**<0.001**	0.77
	Median	34,00	31,00		
	p	0.491	0.717		

SD: standard deviation, **VR:** Virtual reality

Similarly, income level did not yield a significant difference in anxiety scores before and after VR intervention. However, VR significantly reduced anxiety levels in both income groups—those earning below and above the minimum wage—with a moderate effect size observed in each group (Table 5).

Table 5. Anxiety scores according to depending on income levels					
Income Levels		**Before VR**	**After VR**	**p**	**Effect size**
Below minimum wage	Mean	33,89	30,91		
	SD	4,50	3,48	**<0.001**	0.74
	Median	34,00	30,00		
Above minimum wage	Mean	33,24	30,89		
	SD	4,12	3,95	**<0.001**	0.58
	Median	33,50	31,00		
	p	0.539	0.740		

SD: standard deviation, **VR:** Virtual reality

There was no significant difference in preoperative anxiety scores between age groups before and after the use of VR glasses. However, the use of VR glasses prior to surgery significantly reduced anxiety scores in both the 0–39 and over-40 age groups. In both age groups, the preoperative application of VR glasses appeared to have a moderate effect in reducing preoperative anxiety (Table 6).

Table 6. Anxiety scores according to depending on age					
Age group		**Before VR**	**After VR**	**p**	**Effect Size**
0-39	Mean	33,69	31,23		
	S.D.	3,763	3,049	<0.001	0.71
	Median	34,00	31,00		
Over 40	Mean	33,53	30,67		
	S.D.	4,722	4,084	<0.001	0.64
	Median	34,00	30,00		
	p	0.920	0.514		

SD: standard deviation, **VR:** Virtual reality

DISCUSSION

Preoperative anxiety is a common psychological condition observed in patients prior to surgery and may adversely affect the anesthetic and surgical process by enhancing the physiological stress response. This anxiety can be influenced by various factors such as age, gender, previous surgical experience, level of knowledge, and personality traits. This study assessed the effectiveness of virtual reality (VR) in reducing preoperative anxiety among patients undergoing laparoscopic cholecystectomy. The findings demonstrated that VR significantly decreased anxiety scores, with a moderate effect size (d = 0.68). Although a decrease of 1.036 beats per minute in heart rate was observed following the VR intervention, this change was not statistically significant.

Virtual reality is an emerging tool in healthcare with applications in medical education, rehabilitation, and the management of psychological and pain-related conditions (21). It creates an immersive environment that limits the brain's processing of distressing stimuli and has been shown to reduce pain scores more effectively than standard distraction techniques, sometimes by as much as 30%. Previous studies have shown VR to be effective in alleviating pain and anxiety in various clinical contexts, including upper gastrointestinal endoscopy, dental surgery, burn wound care, and labor (22-26).

Pharmacologic agents are frequently used to manage preoperative anxiety and pain, but these drugs can lead to complications such as excessive sedation, hypotension, impaired airway reflexes, and postoperative apnea. These risks underscore the potential value of non-pharmacologic interventions such as VR in minimizing sedative use and reducing adverse outcomes (27-28).

Distraction is a strategy to redirect attention away from the stressor and towards other thoughts and behaviors that are unrelated to the stressor (29). It has been shown that they are effective during medical procedures (30). Virtual Reality is a paradigm shift in how people interact with computers. Instead of looking at a handheld or desk-mounted computer screen, computer screens are mounted on the head. The user wears a VR headset where miniature computer screens are located close to the patients' eyes. Lenses are used to focus images on the patients' eyes to make them feel as if they are inside a 3D computer-generated environment. Immersive VR directly focuses on the patient's individual perception of stressful stimuli and reduces their negative experiences through distraction (31). VR immerses the user in an interactive virtual environment; while allowing the user to actively see the surroundings in 360 degrees, noise-canceling headphones provide suitable film music.

According to the results of our study, using VR application was found to be effective in reducing preoperative anxiety, and there were no differences based on factors such as sex, education, income, and risk group, with anxiety significantly decreasing in each group. In the study by Karancı et al., which aimed to predict the predictors of preoperative anxiety, it was observed that anxiety levels were higher in women. Additionally, the expectation of surgery and the individual's feeling of helplessness have also been found to be significant predictive factors of anxiety (19). In another study, a higher level of education was found to be a factor that increases preoperative anxiety (32).

In a study by Raja et al. investigating the effectiveness of VR application on preoperative anxiety in patients undergoing hernia, appendectomy, tonsillectomy, and hysterectomy surgeries, it was found that patients who experienced an immersive experience before surgery had reduced anxiety levels (33). Additionally, this study emphasized that the increase in preoperative satisfaction provided several benefits and that the virtual reality-based solution is one of the easiest ways for hospitals to adopt.

In a study by Noben et al. involving 97 pregnant patients scheduled for cesarean section, the effect of watching a preoperative VR video on preoperative anxiety was investigated. It was found that the VR application was generally not effective in reducing

anxiety, but it did lower anxiety in women who had previously undergone a cesarean section (34).

In a study by Şahin et al. investigating the effects of progressive muscle relaxation and virtual reality goggles on patient satisfaction and anxiety levels, it was found that both groups showed an increase in satisfaction and a decrease in anxiety compared to the control group (35). In a systematic review examining the effectiveness of audiovisual interventions in reducing preoperative anxiety in children, it was found that in 14 out of the 18 studies reviewed, such interventions reduced children's preoperative anxiety (36).

In a study by Rousseaux et al., where VR applications and VR hypnosis methods were used in cardiac surgery patients and changes in pain and anxiety were investigated, it was found that both techniques were effective in reducing pain and anxiety. It has been stated that the use of these applications in medicine will increase over the years (37). In a study by Ganry et al. investigating the effect of VR applications on preoperative anxiety in maxillofacial plastic surgery patients, it was found that there was a significant reduction in the patients' anxiety levels and salivary cortisol levels after the intervention (38). In a study where surgical simulation was performed using VR applications on children scheduled for surgery, it was observed that the application reduced the children's anxiety levels and was effective (39).

In a meta-analysis study, the effectiveness of VR applications before various types of surgeries in the pediatric group was examined. Pediatric VR research has primarily focused on distraction. It has been stated that VR is an effective distraction intervention for reducing pain and anxiety in pediatric patients undergoing a wide range of medical procedures (40). A VR theater application was performed on 191 pediatric patients the day before surgery. It was observed that there was no significant decrease in anxiety levels during surgery, but there was a significant decrease in postoperative pain levels compared to the control group (41).

Faruki et al. found that VR applications reduced the need for postoperative medication and anxiety level (42). In a randomized controlled prospective study by Ryu et al. investigating the effect of playing games with VR goggles on preoperative anxiety in children, it was found that VR game playing application significantly reduced preoperative anxiety (43). Batuman et al. demonstrated that informative video viewing was effective in reducing preoperative anxiety in the pediatric age group (44). Robertson et al. found that VR applications reduced preoperative anxiety in patients undergoing atroscopic knee surgery (29).

Overall, the findings of our study align with the broader literature, supporting the use of VR as an effective non-pharmacologic intervention for reducing preoperative anxiety.

Our study had some limitations. First, we did not perform psychiatric consultation and mood assessment before surgery. Our study is based on a patient-reported scale. The absence of objective physiological measurements, such as salivary cortisol concentration, and the lack of investigation into the long-term postoperative effects of VR constitute additional limitations of our research.

CONCLUSION

In conclusion, the application of virtual reality (VR) glasses was found to be effective in significantly reducing preoperative anxiety among patients undergoing laparoscopic cholecystectomy. Given its non-invasive and non-pharmacologic nature, VR may serve as a valuable adjunct in preoperative preparation, enhancing patient comfort and potentially reducing the need for sedative medications.

Considering its effectiveness across diverse demographic groups and ease of implementation, VR has the potential to become a widely adopted tool in clinical practice. Further research is warranted to evaluate its long-term benefits and applicability across different surgical populations and clinical settings.

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Impact of CDH1 Mutation Status on Gene Expression and Co-Expression Networks in Stomach Adenocarcinoma

CDH1 Status in Gastric Cancer

Perçin Pazarcı[1]

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Abstract: Objective: This study aims to explore how cadherin 1 (CDH1) mutation status influences gene expression and co-expression networks in Stomach Adenocarcinoma (STAD). By examining frequently mutated genes, we assess transcriptomic alterations and potential molecular rewiring associated with CDH1 mutations.

Method: Somatic mutation profiles and RNA-seq data for STAD patients were obtained from The Cancer Genome Atlas (TCGA). The 20 most frequently mutated genes were identified. Samples were stratified into CDH1-mutated (CDH1+) and non-mutated (CDH1−) groups. Gene expression differences were analyzed using the Wilcoxon rank-sum test. Spearman's correlation was used to construct gene co-expression networks for each group, with significance defined as FDR-adjusted $P \leq 0.05$ and $|\rho| > 0.5$.

Results: Seven genes showed significant differential expression between CDH1+ and CDH1− tumors. Among these, FAT3, SYNE1, ZFHX4, FAT4, and HMCN1 were upregulated in CDH1+ cases, while PCLO and DNAH5 were downregulated. Co-expression network analysis revealed 47 significant gene-pair correlations in CDH1+ tumors versus 19 in CDH1−.

Conclusion: CDH1 mutation status in STAD is associated with distinct gene expression profiles and co-expression patterns, particularly involving genes related to cell adhesion and cytoskeletal organization. These findings highlight the broader impact of CDH1 alterations beyond E-cadherin loss and suggest candidate genes and pathways that may serve as biomarkers or therapeutic targets in CDH1-mutant gastric cancer.

Keywords: CDH1, Correlation network, Gene expression, Stomach adenocarcinoma

[1]Çukurova University, Faculty of Medicine, Department of Medical Biology, Adana, Türkiye

Email: percinpazarci@gmail.com

ORCID iD: 0000-0002-3708-0054

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INTRODUCTION

Despite a decrease in the number of cases in certain parts of the world, gastric cancer continues to be a serious issue as it is still among the most widespread tumors (1). Majority of stomach cancer is made up by a histological type known as Stomach Adenocarcinoma (STAD) which is also characterized by a great molecular variability (2). Diagnosis, prognosis and treatment are difficult due to this diversity, which has led to extensive studies in order to determine its genetic and transcriptomic bases. The emergence of extensive sequencing initiatives like The Cancer Genome Atlas (TCGA) has enabled a thorough molecular analysis of STAD (3). This aids in uncovering various patterns of genetic changes and disrupted signaling pathways. These studies highlight the presence of mutations that occur over and over again in important genes like tumor protein p53 (TP53), AT-rich interactive domain-containing protein 1A (ARID1A), cadherin 1 (CDH1); as well as changes in chromatin remodeling and cell adhesion (4). By so doing, these findings not just clarified how stomach cancer begins but also facilitated the creation of some molecular classifications that reflect more on the nature of tumor (5).

CDH1 is one of the key genes that is known to cause gastric cancer when mutated. E-cadherin is encoded by CDH1 gene and it is a transmembrane glycoprotein that is very crucial in joining epithelial cells together and also for maintaining structure of tissues (6). Mutations in CDH1 are closely associated with the diffuse subtype of gastric cancer, characterized by poorly cohesive tumor cells and a lack of gland formation (7). Such mutations usually cause disruption of intercellular junctions and increased invasiveness, hence worsening prognosis (8). It is crucial to note that there is also an association between germline CDH1 mutations and hereditary diffuse gastric cancer (HDGC) syndrome, emphasizing their importance in both sporadic and familial cases (7). Even though it is known that CDH1 mutations disrupt cell adhesion and lead to loss of epithelial integrity, little is understood about how CDH1 mutations affect the broader genomic profile and gene expression networks in gastric tumors. The available literature mainly discusses individual gene roles or few molecular pathways, thereby creating a knowledge gap on how CDH1 mutation status may affect expression and interaction of commonly mutated genes in STAD (9).

The recent research indicates that CDH1 mutations may determine not only tumor phenotype but also broader molecular programs that can affect treatment and course of the disease (10). For example, other adhesion related genes may have altered expression or compensatory upregulation in structural proteins might occur within CDH1 dysfunctional tumors giving rise to unique molecular subtypes in STAD. Additionally, depending on CDH1 mutation status, gene co-expression networks could provide an indication of unique regulatory interactions relevant for targeted therapy.

Consequently, this research aims to establish the impact of CDH1 mutation on the expression and co-expression profiles of most frequently mutated genes in STAD. The study will compare CDH1+ tumors with CDH1− tumors in order to identify differentially expressed genes and build comparative correlation networks using TCGA information. This approach can determine if CDH1 mutations cause extensive transcriptional changes and molecular rewiring in STAD. Important regulatory hubs and compensatory mechanisms which might be responsible for the behavior of certain subtypes could also be exposed by the results obtained. Through this study, we hope to enhance our knowledge on the molecular diversity of STAD and isolate potential biomarkers or pathways for use in future diagnosis and treatment plans.

METHODS

Data Collection

Somatic mutation profiles and transcriptomic data for TCGA-STAD cases were obtained from TCGA database. Mutation datasets (Simple Nucleotide Variation and Masked Somatic Mutation) were

retrieved using the TCGAbiolinks R package (v2.34.1) (11). RNA-seq data (STAR-counts) and clinical annotations were downloaded via the UCSC Xena platform. All data corresponded to the TCGA-STAD cohort (3). Total 404 samples are evaluated in TCGA-STAD cohort after excluding samples that do not contain CDH1 mutation data or gene expression data for the most mutated 20 genes.

Identification of most mutated genes

Non-silent somatic mutations (i.e., mutations that alter the amino acid sequence of the encoded protein, such as missense, nonsense, frameshift, and splice site mutations) were extracted, and silent mutations were excluded. Mutation frequencies were calculated as the ratio of patients harboring mutations in each gene to the total cohort size. The 20 genes with the highest mutation rates were selected for downstream analyses.

Stratification by CDH1 mutation status

Patients were classified into two subgroups which are CDH1+ (n=38), comprising samples with non-silent mutations in *CDH1*, and CDH1- (n=366), consisting of samples lacking *CDH1* mutations or containing only silent mutations.

Differential gene expression analysis

Expression levels of the top 20 mutated genes were compared between CDH1+ and CDH1− subgroups. Raw RNA-seq counts were log2-transformed (log2[count + 1]) to approximate normality. Differential expression was assessed using the Wilcoxon rank-sum test, with significance thresholds set at *: P≤0.05, **: P≤0.01, and ***: P≤0.001. Results were visualized as boxplots (ggplot2 R package) (12).

Gene correlation network analysis

Pairwise Spearman's rank correlations (ρ) were computed for the 20 mutated genes within each subgroup. Significant correlations were defined as those with false discovery rate (FDR)-adjusted P≤0.05 and absolute correlation strength $|\rho| > 0.5$. Networks were constructed using the igraph R package, where nodes represented genes, edges represented significant correlations, and edge properties (color: red for positive, blue for negative; width: proportional to $|\rho|$) reflected correlation direction and magnitude (13).

Computational tools and statistical analysis

All analyses were performed in R (v4.4.3). Data retrieval and preprocessing utilized TCGAbiolinks and UCSC Xena. Statistical tests were implemented using the Hmisc package (v5.2-3). Visualizations were generated with ggplot2 (v3.5.1) and igraph (v2.1.4).

RESULTS

Analysis of TCGA-STAD data identified the 20 most frequently mutated genes and titin (TTN), TP53, and mucin 16 (MUC16) were marked as top three (Figure 1). Comparative expression analysis between CDH1+ and CDH1- tumors revealed 7 significantly differentially expressed genes (P≤0.05) (Figure 2): five upregulated in CDH1+ samples [FAT atypical cadherin 3 (FAT3), spectrin repeat containing nuclear envelope protein 1 (SYNE1), zinc finger homeobox 4 (ZFHX4), FAT atypical cadherin 4 (FAT4), and hemicentin 1 (HMCN1)] and two downregulated [piccolo presynaptic cytomatrix protein (PCLO) and dynein axonemal heavy chain 5 (DNAH5)]. 13 genes showed no significant expression difference between groups. Finally, the correlation network constructed based on the expression data of the 20 most frequently mutated genes in CDH1+ and CDH1- samples is presented in Figure 3. All data have been provided in the supplementary material section.

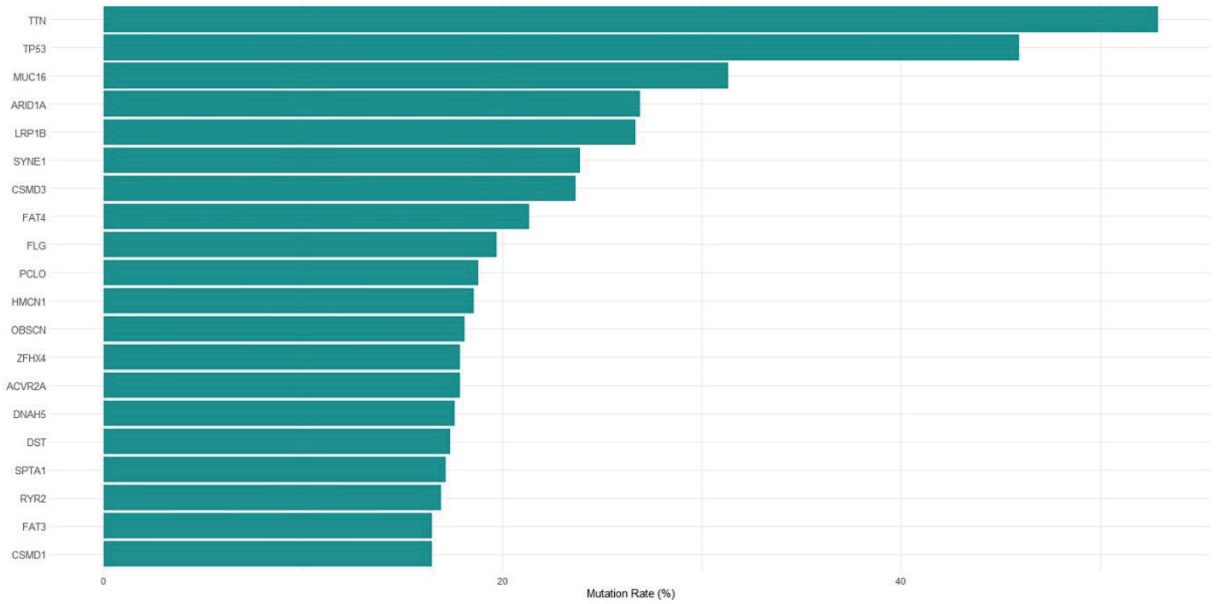

Figure 1. *The most frequently mutated 20 genes in the TCGA-STAD cohort.*

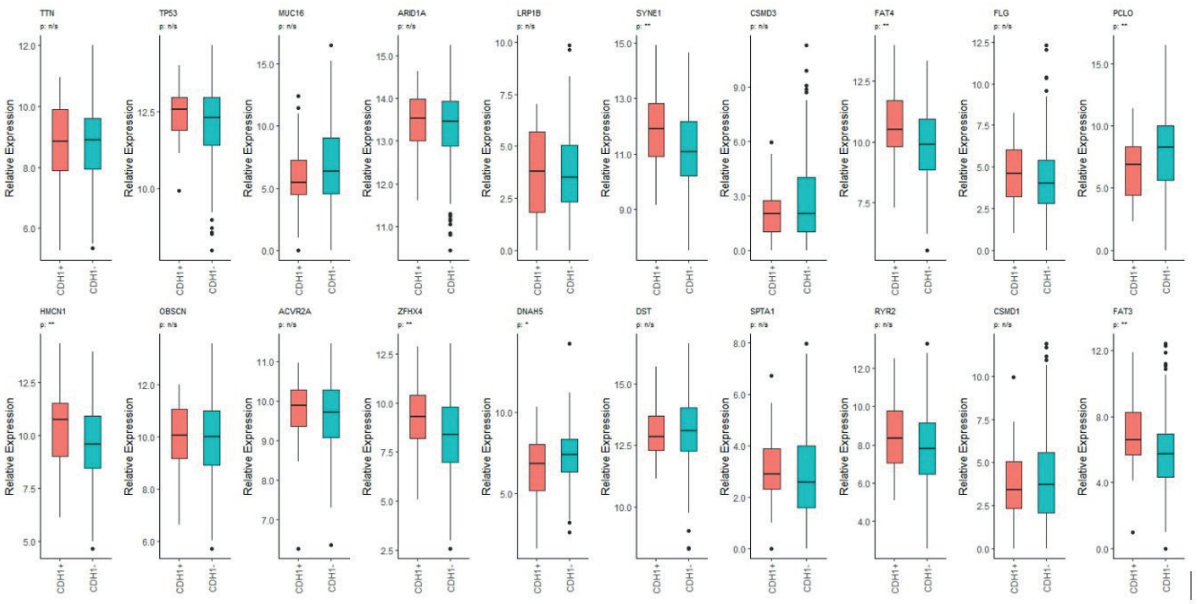

Figure 2. *Comparison of expression levels of the most frequently mutated 20 genes between CDH1+ and CDH1− samples in the TCGA-STAD cohort (*: P≤0.05, **: P≤0.01, ***: P≤0.001, n/s: Not Significant).*

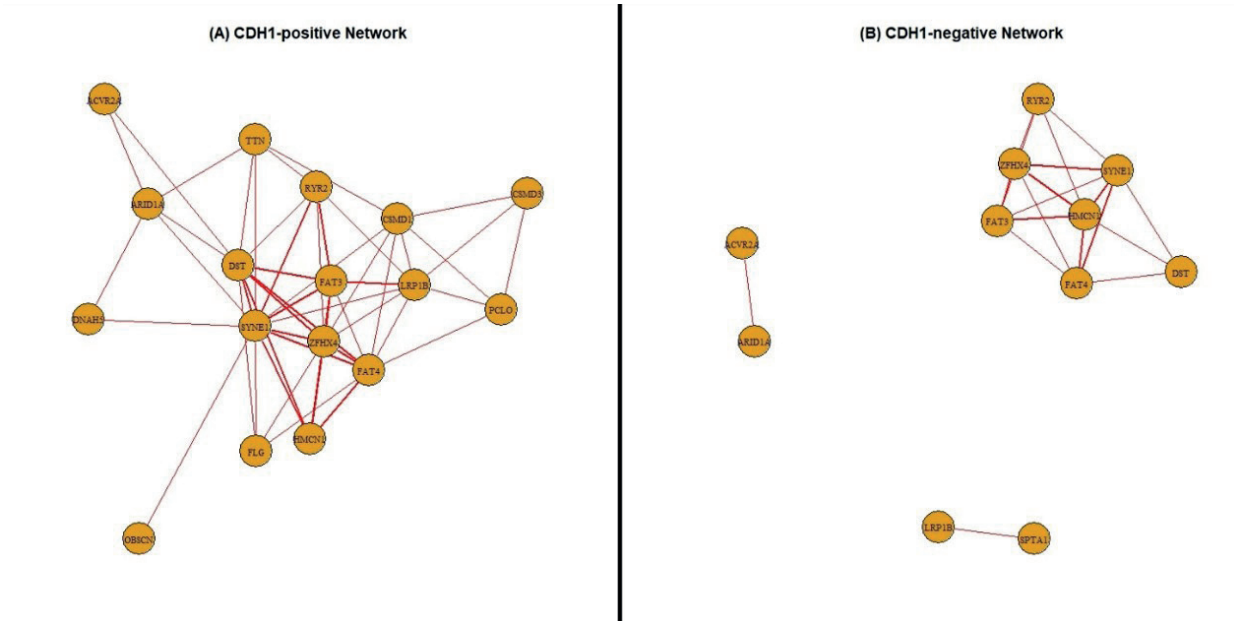

Figure 3. *Gene correlation networks of the most frequently mutated 20 genes in the TCGA-STAD cohort: (A) for CDH1+ samples, (B) for CDH1− samples (Positive correlations are shown in red, negative correlations in blue. Line thickness is proportional to the strength of the correlation coefficient).*

DISCUSSION

The mutational landscape of Stomach Adenocarcinoma (STAD) shows some distinct features that are in line with what we know about how gastric cancer develops. The TTN gene had the highest number of mutations in all cases examined. Although the TTN is very large and therefore prone to random mutations (as it encodes for titin, the largest known protein), there is emerging data that these changes could affect tumor progression through the mechanical properties of cancer cells. TP53 followed closely having mutations in around half of cases analyzed. It is a key cancer suppressor gene that when deactivated causes many cancer types including gastric cancer. Disruption of TP53 leads to resistance of apoptosis, and cells continue dividing even with unstable genomes (14).

The mutation rate of MUC16 is especially curious within the context of gastric cancer, given that this gene codes for CA-125, a glycoprotein related to cell adhesion (15). Loss of epithelial integrity may be enhanced by mutations in this gene, thereby promoting invasion and metastasis (16). The high prevalence of ARID1A mutations underscores the role chromatin remodeling dysregulation plays in STAD pathogenesis since ARID1A is a component of the SWI/SNF complex that controls gene expression by moving nucleosomes around (17). Another commonly changed gene is LDL receptor-related protein 1B (LRP1B) which functions in endocytosis and is linked to resistance when inactivated, hence conferring on tumor cells survival advantages (18). In addition, the fact that many of the highly mutated genes (FAT4, FAT3, DST, SYNE1) code for adhesion and structural proteins indicates that the breakdown of tissue structure is a key aspect in the development of gastric cancer (19). Such changes are expected to compromise contact inhibition and enhance invasiveness.

It is important to note that some commonly mutated genes follow certain patterns that are in line with the TCGA's proposed molecular classifications of gastric cancer, especially the genomically stable and chromosomal instability subtypes (3). The mutational profile is important for comparing

CDH1+ vs CDH1- samples since some of the highly mutated genes are known to interact with or work within CDH1-related pathways. CDH1 is a gene that codes for E-cadherin, which is an important molecule for cell adhesion but usually disrupted in diffuse type of gastric cancer (8). These interactions might expose separate biological pathways and susceptibility profiles particular to CDH1 status in gastric cancer.

The comparison of gene expression profiles in CDH1+ and CDH1- STAD indicates some interesting differences in the way the genes are expressed. These differences may have an impact on the nature of the disease and its outcome in patients. Among the top 20 most frequently mutated genes in STAD, there was a significant difference in 7 when cross-referenced with the CDH1 status ($P \leq 0.05$). It is important to note that out of these 7 genes, 5 (FAT3, SYNE1, ZFHX4, FAT4, and HMCN1) were observed to have increased expressions while 2 (PCLO and DNAH5) had reduced expressions in the CDH1+ subgroup.

The biggest difference was seen in FAT3, which belongs to the cadherin superfamily and is involved in cell adhesion and polarity (20). The observed increase in FAT3 expression in CDH1+ tumors may represent a compensatory effect whereby heightened FAT3 levels serve to partially re-establish the compromised adhesive properties linked with abnormal E-cadherin function. In the same way, FAT4 also showed high levels of expression in relation to CDH1+ samples. These FAT cadherin genes are upregulated together showing a collective response in the cell adhesion network, a probable feature of CDH1+ STAD (19,21).

CDH1+ tumors also had elevated levels of expression for SYNE1 and ZFHX4. SYNE1 codes for a nuclear envelope protein linking nucleoskeleton and cytoskeleton while ZFHX4 acts as a transcription factor involved in neuronal differentiation (22,23). The fact that they are upregulated indicates changes in nuclear structure and gene regulation particular to CDH1+ STAD (24). On top of that, HMCN1 gene, which is responsible for coding an extracellular matrix protein that aids in cell adhesion, portrayed increased expression in CDH1+ samples thereby underlining extensive cell-cell and cell-matrix interaction remodeling in this group (25).

On the other hand, CDH1+ tumors showed significant under-expression of PCLO and DNAH5. Neuronal function is the main function of the cytoskeletal protein that is encoded by PCLO, whereas DNAH5 encodes a component found in ciliary dynein motors. The decrease in their expression could be attributed to changes in cytoskeletal structure and reduced cell motility of CDH1+ STAD, which may affect its invasive and metastatic potential when compared to CDH1- tumors (26,27).

It is interesting to note that some of the highly mutated genes like TTN, TP53 and MUC16 had no significant difference in expression with relation to CDH1 status despite their known roles in STAD (24). This implies that even though STAD patients experience mutations of these genes with high frequency irrespective of CDH1 status, their transcriptional regulation may not be influenced by CDH1 related pathways (28). The observed similarities in the expression levels of important tumor suppressors such as TP53 and ARID1A across both CDH1+ and CDH1- subtypes indicate that these crucial cancer driver genes might act through analogous but different downstream effectors (29).

Another analysis was done on the correlation network of highly mutated genes in STAD. There was a great disparity in the way the genes are transcribed between CDH1+ and CDH1- tumors, which helps us understand better the unique molecular structures of these tumors. For CDH1+ tumors, we found a very tight co-expression network with 47 significant gene-pair correlations (FDR-adjusted $P \leq 0.05$, $|\rho| > 0.5$), as compared to only 19 in the CDH1- subgroup. The observed large difference in network complexity implies that CDH1+ STAD might experience very strict transcriptional control that could be linked to some extent with compensatory effect related to abnormal E-cadherin function (30).

In CDH1+ tumors, co-expression analysis unveiled multiple tight clusters of genes. The hub genes were noted to be SYNE1, FAT4, and ZFHX4, each of them showing strong relationships with no less than 7 other genes across the network. A very high correlation between HMCN1 and ZFHX4 (ρ=0.886) is seen which may imply an interaction between ECM organization and transcriptional regulation (22,25). High positive correlation seen in CDH1+ context between FAT4 and HMCN1 (ρ=0.842), SYNE1 and DST (ρ=0.852), as well as ZFHX4 and FAT4 (ρ=0.819) is also worth noting. These correlations indicate tightly coordinated expression patterns involving cell adhesion, cytoskeletal architecture, and nuclear organization in the CDH1+ tumors (31). Although the CDH1- tumors demonstrated fewer significant correlations, they maintained several key gene associations (such as SYNE1, FAT4, HMCN1, and ZFHX4) observed in CDH1+ tumors. The fact that these basic correlations remained intact across the two subtypes implies that they play a crucial role in STAD development independent of CDH1 mutation status. However, the strength of these correlations generally appeared reduced in CDH1- tumors.

It is important to note that some gene correlations seen in CDH1+ tumors were missing in the CDH1- subgroup. For example, TTN had positive correlation with 5 genes [ARID1A, SYNE1, DST, ryanodine receptor 2 (RYR2), CUB and Sushi multiple domains 1 (CSMD1)] in CDH1+ but not in CDH1-, which implies this commonly mutated gene might have a CDH1 dependent role in gastric carcinogenesis (32). Similarly, CUB and Sushi multiple domains 3 (CSMD3) demonstrated significant correlations with LRP1B, PCLO, and CSMD1 only in CDH1+ tumors, indicating potential functional relationships that are specific to this STAD subtype (33).

Conversely, there was a strong connection between LRP1B and spectrin alpha erythrocytic 1 (SPTA1) (ρ=0.518) in the CDH1- subgroup which was missing in CDH1+ tumors. Perhaps, this kind of correlation arises due to adaptive responses which are turned on only when E-cadherin does not work properly (9). The fact that these two STAD subtypes have dissimilarly high or low expression profiles for certain genes implies that they are inherently distinct at the molecular level, and this may have a role in why they differ so much with regard to treatment outcome as well as prognosis (9).

It is interesting that genes responsible for cell adhesion and cytoskeletal organization intertwined to form closely linked modules in the two subgroups, although they were arranged differently. In CDH1+ tumors, these modules included extensive correlations with nuclear envelope components (SYNE1) and transcriptional regulators (ZFHX4) (22,23). This suggests coordinated regulation of cell architecture and gene expression. The fact that there were tight correlations between SYNE1, FAT4, HMCN1, and ZFHX4 in both categories underlines the importance of cell adhesion and nuclear-cytoskeletal links in STAD progression (34). The subtype-specific differences in these coordination patterns may contribute to the distinct invasive behaviors associated with CDH1 status (35).

Limitations of the study

This study is limited by its reliance on TCGA data and lack protein-level information in its current form. The co-expression findings require experimental validation. Additionally, the CDH1-based grouping does not fully capture tumor heterogeneity or account for other genetic drivers.

CONCLUSIONS

This study reveals that STAD has unique characteristics depending on CDH1 mutation status, which go beyond mere E-cadherin malfunction. Genes related to nuclear structure, cytoskeletal organization, and cell adhesion exhibit varied expression patterns and co-expression interactions, suggesting that CDH1 status affects more cellular functions than previously thought. These results are important for the clinic since they could explain the different behaviors and treatment reactions of diffuse and intestinal STAD subtypes. Future treatment strategies specifically designed to target

identified hub genes and pathways might provide more successful treatments for patients depending on patients' CDH1 status. Furthermore, the above-mentioned strong correlations between specific genes can be used as possible biomarkers for forecasting the beginning of disease and treatment response. Bridging the present genomic information into enhanced clinical management of gastric cancer patients will require more research on the functional implications of the molecular variations found in this study.

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Evaluation of the Effect of Axial Length on Foveal Microstructure: A Comparative Optical Coherence Tomography Angiography Study

Comparative OCTA of Foveal Microstructure

Fatih Kahramanoğlu[1], Emine Alyamaç Sukgen[2], Muzaffer Talha Albayrak[3]

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Abstract: Objective: Myopia, characterized by an increase in the eye's axial length, is a common refractive error that can lead to degenerative changes in the retina and optic nerve. The purpose of this study was to evaluate the effects of different axial length (AL) values on retinal and optic nerve head structures using Optical Coherence Tomography (OCT) and Optical Coherence Tomography Angiography (OCT-A).

Method: This prospective cross-sectional study, included 150 patients (150 eyes) with cataracts, aged between 18 and 69 were. Patients were divided into five groups based on their AL values. Following ophthalmological examination, retinal nerve fibre layer (RNFL) and ganglion cell complex (GCC+IPL) thicknesses were measured with OCT, while foveal and peripapillary vascular density were measured with OCT-A. The obtained data were statistically compared among the AL groups.

Results: The study revealed a significant thinning of RNFL and GCC+IPL thicknesses as AL increased ($p<0.05$). This thinning was particularly prominent in the nasal and inferior quadrants of the RNFL, and in the inferonasal and superotemporal quadrants of the GCC+IPL. In vascular density measurements, an increase in superficial and deep foveal density (SFD and DFD) values was observed as AL increased ($p<0.05$). This is thought to be due to the optical magnification effect caused the increade in axial length. No significant correlation was found between foveal avascular zone (FAZ) area and AL. Our findings supported that increasing axial length lead to thinning of neural tissue thicknesses of the retina and optic nerve, and this condition was associated with mechanical stress. The increase of vascular density detected in OCT-A measurements might be due to artefacts, indicating that caution should be exercised in the evaluating of vascular changes related to myopia.

Conclusion: This study confirms that axial elongation in myopia leads to thinning of the retinal neural tissues. Advanced imaging methods such as OCT and OCT-A are important tools for evaluating structural and vascular changes in myopic patients and for identifying potential complications at an early stage.

Keywords: Optical coherence tomography angiography, Myopia, Axial length.

[1]MD, Department of Ophthalmology, Adana City Training & Research Hospital, Adana, Türkiye
Email: kahramanoglu.md@gmail.com
ORCID iD: 0009-0003-7134-0125

[2]Department of Ophthalmology, Private Medical Clinic, Adana, Türkiye
Email: esukgen@gmail.com
ORCID iD: 0000-0002-2315-434X

[3]Department of Ophthalmology, Kayseri State Hospital, Kayseri, Türkiye
Email: mtalhalbayrak@gmail.com
ORCID iD: 0000-0001-7912-7554

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INTRODUCTION

Myopia is defined as a refractive error where parallel light rays entering the eye at rest are focused in front of the retina (1). Myopia is a widespread refractive error in the general population with a wide range of aetiology. There are many causes for the etiology of myopia. It is divided into two types according to its etiopathogenesis. If the axial lenght(AL) of the eye is longer than average, this defect is called axial myopia. If the refractive power of the eye is higher than normal, it is called refractive myopia (2). With the increase in AL, the retina, especially the posterior pole, shows microstructural degenerative changes. Myopia is a risk factor for various retinal pathologies, including retinal detachment, macular holes, choroidal neovascularisation, and retinoschisis. Myopia-related complications are among the leading causes of visual impairment (3).

Axial length is measured with A-scan biometry. The axial eye length of an adult human is mostly between 22 and 24.5 mm, with an average length of 23.6 mm (4). The difference in AL between the two eyes is generally not expected to exceed 0.3 mm (5).

Recently, OCT (SS-OCT) and Optical Coherence Tomography Angiography (OCTA) have gained clinical popularity. OCTA is a non-invasive imaging method that offers high resolution in visualising vascular changes. OCT is widely used in clinical and academic ophthalmology and has become indispensable in the diagnosis and treatment of high myopia and its complications with high-resolution cross-sectional retinal images (6). OCT allows measurements of the peripapillary retinal nerve fibre layer (RNFL) thickness analysis of the optic nerve head, macula and ganglion cell (GCA).

Early detection of changes in the intraretinal structures of a myopic eye is crucial. Identifying abnormal patterns of retinal structures will helps in evaluating early-stage, myopia-related complications (3).

The purpose of this study was to evaluate the effects of the increase in the eye's axial length on the retinal nerve fibre layer, ganglion cell complex, and optic nerve head blood supply with OCT and OCT-A

MATERIALS AND METHODS

This prospective cross-sectional study was conducted at the Adana City Training and Research Hospital between June 2020 and June 2021. A total of 150 eyes of 150 patients who presented to the Ophthalmology Clinic of Adana City Training and Research Hospital for cataracts were included in the study. This patient group was selected to adhere to ethical principles and avoid incurring additional healthcare costs, as they frequently undergo Optical Coherence Tomography Angiography (OCTA) as part of their routine clinical assessment.

Approval for this study was obtained from the Adana City Training and Research Hospital Clinical Research Ethics Committee (Date: 17.06.2020, Meeting No: 59, Decision No: 947). Informed consent was obtained from all patients. The study adhered to the principles of the Declaration of Helsinki, and no conflicts of interest were declared.

The inclusion criteria were: age between 18 and 69 years, willingness to participate in the study, no history of ocular diseases other than cataracts, and the ability to achieve adequate pupillary dilation and fixation for OCTA imaging.

Exclusion criteria included a history of ocular trauma or surgery; age under 18 or over 69; history of ocular diseases such as uveitis, glaucoma, tumors, or any retinal pathology; systemic diseases that could affect the vascular structure, such as diabetes mellitus, hypertension, coronary artery disease, or vasculitis; corneal surface problems; media opacities, such as significant lens denseness, that would reduce image quality and preclude accurate measurements; intraocular pressure outside the range of 12-20 mmHg; OCTA and OCT image signal strength (scan quality) below 6/10; pregnancy; a history of systemic or ocular medication use; and a history of smoking, alcohol, or substance abuse.

During data collection, the age, sex, and the studied eye of each participant were recorded. The ophthalmological examination included

measurement of best-corrected visual acuity (BCVA) using a Snellen chart (expressed as a decimal value), measurement of intraocular pressure (IOP) with applanation tonometry, and a fundoscopic examination following pupillary dilation. This was performed using a +90 D non-contact lens to screen the optic disc, macula, and peripheral retina for any degeneration, lesions, or other pathologies. Following the examination, optical biometry (IOLMaster, Carl Zeiss AG, Germany), OCTA (AngioVue RTVue-XR, Optovue, Inc.; Fremont; California, USA) and OCT examination (Carl Zeiss Meditec, Inc., CA) were performed.

Based on the AL values obtained from biometry, participants were divided into five groups:

Group 1: AL < 22 mm

Group 2: AL 22.00–22.99 mm

Group 3: AL 23.00–23.99 mm

Group 4: AL 24.00–24.99 mm

Group 5: AL ≥ 25 mm

Studies in the literature have used groupings with 1 mm, 1.5 mm, and 2 mm differences. Narrower intervals facilitate the detection of subtle changes in parameters related to AL, Therefore, a 1 mm interval was used for grouping in our study (7,8,9,10,11).

The biometric measurements of the patients, including axial length (AL), anterior chamber depth (ACD), and keratometry values, were measured using the IOL-Master (Carl Zeiss Meditec, La Jolla, CA, USA).

OCTA scans were performed using the AngioVue® (RTVue-XR, Fremont, California, USA) device, a dual-modality OCT system that provides both structural and vascular measurements. For all patients, fovea-centered 3x3 mm macular scans and 4.5x4.5 mm optic disc scans were acquired and evaluated. However, the OCTA device used in this study lacks a magnification correction feature, which can lead to deviations in patients with axial lengths above and below 23.95 mm.

Vascular density (%) was measured in the superficial and deep capillary plexuses within an area divided by 1 mm and 3 mm diameter circles centered on the foveal avascular zone (FAZ), corresponding to the foveal and parafoveal regions. Each region was also divided into four equal quadrants: temporal, superior, nasal, and inferior.

Central macular thickness was automatically measured by the device by selecting the Quickvue module, which calculates the distance between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE). The 3x3 mm scan was segmented into a 1 mm central foveal ring and a surrounding concentric ring divided into four quadrants (totaling 5 zones).

For the optic nerve head, whole image vessel density, inside disc vessel density, and peripapillary capillary vascular density (PPCVD) were calculated by the software. In our study, whole image density, inside disc density, peripapillary density (PPD), PPD for the inferior and superior hemispheres, and PPD for the superior, temporal, inferior, and nasal quadrants were calculated. Additionally, to evaluate the microvascular structure, the capillary vessel densities within these measurement areas were used as a study parameter. In the optic disc mode, the peripapillary retinal nerve fibre layer thickness (pRNFLT) within a 3.45 mm diameter circle around the optic disc was also evaluated.

GCA was performed in six sectors around the macula: superotemporal, superior, superonasal, inferonasal, inferior, and inferotemporal.

Statistical analysis of the data was performed using the SPSS (Statistical Package for the Social Sciences) version 23.0 software package. Categorical measurements were summarized as numbers and percentages, while continuous measurements were summarized as mean and standard deviation (or median and minimum-maximum where appropriate). The Shapiro-Wilk test was used to determine whether the parameters followed a normal distribution. For comparisons between groups, the One-way ANOVA test was used for normally distributed parameters, and the Kruskal-Wallis test was used for non-normally distributed

parameters. To identify the source of intergroup differences, the Bonferroni test was used as a post-hoc test for normally distributed parameters with equal variances, while Dunn's test with Bonferroni correction was used as a post-hoc test for non-normally distributed parameters. A p-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

One hundred fifty eyes of 150 patients were included in our study. A total of 150 patients were included, with 30 patients in each group based on their axial lengths: under 22 mm, 22-22.99 mm, 23-23.99 mm, 24-24.99 mm, and 25 mm and above. It was determined that 51.3% (n=77) of the patients were male and 48.7% (n=73) were female. The average age of the patients was found to be 44.3±11.1 years (Min: 18, Max: 69). The eye included in the study was the right eye in 53.3% (n=80) of the patients and the left eye in 46.7% (n=70). The mean axial length was observed to be 23.56±1.61 (Min: 19.72, Max: 27.12) in the patients.

Table 1 summarizes the findings obtained from the average OCT-A measurements of all patients included in the study.

Table 1. Average FAZ, AI, FD, CMT values, and average OCT-A measurements of the optic disc and its surroundings for all patients.

Parameter	Mean±sd	Med (Min-Max)
Faz	0,29 ± 0,09	0,28 (0,05-0,55)
AI	1,13 ± 0,04	1,13 (1,06-1,26)
FD	51,89 ± 3,82	52,18 (39,66-60,05)
CMT	218,25 ± 17,64	216 (181-276)
Whole Image (%)	50,55 ± 3,42	50,4 (43,3-80)
Inside disc (%)	51,94 ± 5,45	53,4 (34,6-64,2)
PPCVD (%)	52,41 ± 2,76	52,3 (44,4-58,4)
Superior Half PPCVD	52,69 ± 2,83	53 (44-61)
Inferior Half PPCVD	52,35 ± 4,41	52 (42-90)
Superior PPCVD	52,12 ± 4,54	52 (32-63)
Temporal PPCVD	50,66 ± 5,22	52 (33-61)
Inferior PPCVD	53,65 ± 3,64	54 (43-63)
Nasal PPCVD	53,79 ± 5,49	53 (42-68)

FAZ: Foveal avascular zone AI: Acircularity Index FD: Foveal density CMT: Central macular thickness PPCVD: Peripapillary capillary vascular density

Table 2 shows that the groups were similar in terms of the demographic characteristics examined (gender, studied eye, and age).

Table 2. Comparison of Demographic Characteristics of the Groups

	<22 mm (a)	22-22,99 mm (b)	23-23,99 mm (c)	24-24,99 mm (d)	>25 mm (e)	p
	n(%)	n(%)	n(%)	n(%)	n(%)	
Sex						
Male	17 (56,7)	16 (53,3)	16 (53,3)	14 (46,7)	17 (56,7)	0,938
Female	13 (43,3)	14 (46,7)	14 (46,7)	16 (53,3)	13 (43,3)	
Eye						
Right Eye	14 (46,7)	14 (46,7)	14 (46,7)	22 (73,3)	13 (43,3)	0,118
Left Eye	16 (53,3)	16 (53,3)	16 (53,3)	8 (26,7)	17 (56,7)	
	Mean±sd	**Mean±sd**	**Mean±sd**	**Mean±sd**	**Mean±sd**	**p**
Age	43,27±10,68	47,07±12,39	43,97±12,22	47,90±10,58	39,33±7,19	0,109

* p<0,05, chi square test, Oneway Anova test, Bonferroni test

In Table 3, the differences between the groups were examined with OCT-A measurements. The analysis found that the differences in SPD (p=0.168), TEMPORAL SPD (p=0.147), SUPERIOR SPD (p=0.153), NASAL SPD (p=0.676), and INFERIOR SPD (p=0.365) measurements between the groups were not statistically significant (p>0.05). A significant difference was detected between the groups in the SFD (p=0.005) value (p<0.05) (Table 3).

The source of the difference found in the SFD value was that patients with an AL of 25 mm and above had a higher measurement value compared to the patients in the 22-22.99 mm and 23-23.99 mm groups (p<0.05) (Table 3).

Table 3. Examination of Differences Between Groups with OCTA Superficial Vascular Density Measurements

	<22 mm (a)	22-22,99 mm (b)	23-23,99 mm (c)	24-24,99 mm (d)	>25 mm (e)	p	Post Hoc p
SFD (F)	16,800 [9,55]	14,250 [4,80]	14,800 [7,65]	15,050 [8,90]	19,900 [5,78]	**0,005**	e-b; p=0,007 e-c; p=0,010
SPD (χ2)	50,700 [2,88]	51,450 [3,70]	52,400 [3,98]	52,400 [3,52]	52,400 [6,13]	0,168	
TEMPORAL SPD (χ2)	48,800 [3,27]	49,250 [4,12]	50,400 [4,68]	49,800 [2,88]	50,100 [4,30]	0,147	
SUPERIOR SPD (χ2)	52,300 [3,85]	53,400 [3,00]	53,450 [4,63]	53,450 [4,45]	54,950 [5,72]	0,153	
NASAL SPD (χ2)	50,150 [4,85]	50,650 [3,85]	51,050 [4,10]	51,00 [4,95]	51,850 [7,87]	0,676	
INFERIOR SPD (χ2)	52,650 [2,40]	52,700 [4,25]	53,150 [3,30]	53,050 [4,08]	53,450 [5,90]	0,365	

*p<0.05, **χ2:** Kruskal-Wallis test, **F:** Oneway ANOVA test, Post Hoc Bonferroni and Tamhane's T2 tests

In Table 4, the differences between the groups were examined with OCT-A measurements. The analysis found that the differences in DPD (p=0.335), TEMPORAL DPD (p=0.662), SUPERIOR DPD (p=0.117), NASAL DPD (p=0.641), and INFERIOR DPD (p=0.297) measurements between the groups were not statistically significant (p>0.05). A significant difference was detected between the groups in the DFD (p=0.016) value (p<0.05) (Table 4).

The source of the difference found in the DFD value was that patients with an AL of 25 mm and above had a higher measurement value compared to the patients in the 22-22.99 mm and 23-23.99 mm groups (p<0.05) (Table 4).

Table 4. Examination of Differences Between Groups with OCTA Deep Vascular Density Measurements

	<22 mm (a)	22-22,99 mm (b)	23-23,99 mm (c)	24-24,99 mm (d)	>25 mm (e)	p	Post Hoc p
DFD (F)	34,500 [14,72]	31,100 [9,08]	33,050 [9,68]	34,700 [10,93]	38,400 [8,20]	**0,016**	e-b; p=0,032 e-c; p=0,033
DPD (χ2)	55,850 [4,82]	56,750 [5,12]	57,300 [3,40]	56,350 [4,58]	57,050 [5,38]	0,335	
TEMPORAL DPD (F)	56,200 [4,80]	57,150 [4,72]	56,500 [3,88]	56,650 [4,55]	56,950 [3,60]	0,662	
SUPERIOR DPD (χ2)	56,00 [5,78]	57,400 [5,85]	57,400 [4,00]	54,95 [5,00]	57,35 [6,38]	0,117	
NASAL DPD (χ2)	56,55 [4,23]	57,50 [4,63]	57,60 [3,38]	56,85 [4,90]	57,75 [4,85]	0,641	
INFERIOR DPD (χ2)	56,05 [5,00]	56,95 [4,43]	57,35 [4,52]	56,35 [5,68]	56,50 [6,47]	0,297	

*p<0.05, **χ2:** Kruskal-Wallis test, **F:** Oneway ANOVA test, Post Hoc Bonferroni and Tamhane's T2 tests

In the GCL+IPL measurements presented in Table 5, it was found that the differences between the groups were significant for the average (p<0.001), superior (p<0.001), superotemporal (p<0.001), inferotemporal (p=0.001), inferior (p=0.007), inferonasal (p<0.001), and superonasal quadrant (p=0.002) values (p<0.05).

It was found that the observed differences in the average and inferonasal quadrant GCL+IPL measurements were due to the fact that patients with an AL of 25 mm and above had lower values than those with an AL of under 22 mm and in the 22-22.99 mm group (p<0.05).

The source of the difference found in the GCL+IPL superior quadrant was that patients with an AL under 22 mm had higher values than those with an AL in the 23-23.99 mm group and 25 mm and above group (p<0.05).

The source of the difference observed in the superotemporal (p<0.001) and inferotemporal (p=0.001) quadrant measurements obtained from GCL+IPL measurements was determined to be that those with an AL of 25 mm and above had lower values than those with an AL of under 22 mm, between 22-22.99 mm, and between 23-23.99 mm (p<0.05).

The source of the observed difference in the inferior and superonasal quadrant measurements was determined to be that those with an AL of under 22 mm had higher values than those with an AL of 25 mm and above (p<0.05) (Table 5).

Table 5. Examination of Differences Between Groups with GCL+IPL Measurements

	<22 mm (a)	22-22,99 mm (b)	23-23,99 mm (c)	24-24,99 mm (d)	>25 mm (e)	p	Post Hoc p
GCL+IPL MEAN (F)	87,5 [7,5]	84,5 [8]	84,5 [18]	85 [5,25]	80 [10]	**<0,001**	a-e; p<0,001 b-e; p=0,039
GCL+IPL S (F)	88 [9]	85,5 [8,25]	84 [9]	85,5 [5,25]	82 [9]	**<0,001**	a-c; p=0,013 a-e; p<0,001
GCL+IPL ST (F)	86,5 [7,75]	84 [8]	82,5[6,5]	85,5 [7]	79 [8,5]	**<0,001**	a-e; p<0,001 b-e; p=0,003 c-e; p<0,001
GCL+IPL IT (F)	83,5 [8,75]	81 [8,25]	81 [7,25]	82,5 [6,25]	79 [9]	**0,001**	a-e; p<0,001 b-e; p=0,030 c-e; p=0,016
GCL+IPL I (χ2)	88,5 [11,5]	85 [9,5]	83,5 [7,25]	83 [7,25]	79 [12]	**0,007**	a-e; p=0,039
GCL+IPL IN (χ2)	87 [9,75]	83,5 [5,25]	84,5 [8,25]	84 [6,25]	80 [8]	**<0,001**	a-e; p=0,001 b-e; p=0,012
GCL+IPL SN (F)	88,5 [10,75]	86,5 [7,25]	85 [9,5]	85 [7,25]	79 [11]	**0,002**	a-e; p=0,001

*p<0.05, **χ2:** Kruskal-Wallis test, **F:** Oneway ANOVA test, Post Hoc Bonferroni and Tamhane's T2 tests **GCL+IPL:** Ganglion cell layer and inner plexiform layer, **AVG:** average, **S:** superior, **ST:** superotemporal, **IT:** inferotemporal, **I:** inferior, **IN:** inferonasal, **SN:** superonasal

In Table 6, the differences in RNFL thickness measurements between the groups were examined. The analysis found that the differences in PPRNFL (p<0.001), superior half (p=0.002), inferior half (p<0.001), superior quadrant (p=0.009), temporal quadrant (p=0.026), inferior quadrant (p<0.001), and nasal quadrant (p<0.001) values between the groups were statistically significant (p<0.05) (Table 6). When the source of the difference between the groups in RNFL thickness measurements was examined:

The difference observed in the PPRNFL value was found to be due to those with an axial length of less than 22 mm having a higher value than those with an axial length of 23-23.99 mm (p=0.002) and 25 mm and above (p=0.021); it was also found that those with an axial length between 22-22.99 mm had a higher value than those between 23-23.99 mm (p=0.033) (p<0.05).

The source of the difference found in the RNFL superior half and superior quadrant values was determined to be that those with an axial length of less than 22 mm had a higher value than those with an axial length of 23-23.99 mm (p<0.05).

The difference found in the RNFL inferior half value was determined to be due to those with an AL of less than 22 mm having a higher value than those with an AL of 23-23.99 mm (p=0.005) and 25 mm and above (p=0.012) (p<0.05).

The source of the difference found in the RNFL temporal quadrant value was determined to be that those with an AL between 23-23.99 mm had a lower value than those with an AL of less than 22 mm (p=0.047) and those between 24-24.99 mm (p<0.05).

The source of the difference observed in the RNFL inferior quadrant value was found to be due to those with an AL of less than 22 mm and those between 22-22.99 mm having a higher value than those with an AL of 23-23.99 mm and 25 mm and above (p<0.05).

In the differences detected between the groups with the RNFL nasal quadrant value, it was found that those with an AL of less than 22 mm had a higher value than those with an AL of 23-23.99 mm, 24-24.99 mm, and 25 mm and above (p<0.05).

Table 6. Examination of Differences Between Groups with RNFL Thickness Measurements

	<22 mm (a)	22-22,99 mm (b)	23-23,99 mm (c)	24-24,99 mm (d)	>25 mm (e)	p	Post Hoc p
PPRNFL(µm)	108,00 [22,50]	101,000 [18,25]	94,500 [12,5]	97,00 [13]	94,50 [14,50]	**<0,001**	a-c; p=0,002 a-e; p=0,021 b-c; p=0,033
Superior Half	105,00 [16,25]	101,00 [15,25]	93,00 [14,25]	97,50 [8,50]	95,00 [17,00]	**0,002**	a-c; p=0,007
Inferior Half	109,00 [24,75]	100,00 [17,50]	93,00 [16,50]	97,00 [16,25]	94,500 [11,00]	**<0,001**	a-c; p=0,005 a-e; p=0,012
Superior	124,5 [86,181]	123 [85,179]	109,5 [84,146]	117 [93,150]	111,5 [88,140]	**0,009**	a-c; p=0,041
Temporal	66,0 [18,75]	67,0 [16,25]	61,0 [10,50]	67,0 [13,25]	67,0 [12,75]	**0,026**	a-c; p=0,047 d-c; p=0,035
Inferior	137,50 [29,50]	135,00 [26,50]	118,50 [19,75]	125,500 [22,25]	116,500 [18]	**<0,001**	a-c; p=0,046 a-e; p=0,012 b-c; p=0,031 b-e; p=0,005
Nasal	99,00 [20,50]	93,00 [20,0]	82,50 [22,0]	82,50 [17,50]	84,00 [24,50]	**<0,001**	a-c; p=0,002 a-d; p=0,003 a-e; p=0,025

DISCUSSION

The aim of this study is to evaluate the effects of AL on different ocular structures using OCT-A. Our findings show that increased AL, which is associated with higher degrees of myopia, leads to significant changes in the microvascular structures of the retina and optic nerve head, as well as in neural tissue thicknesses. These results are consistent with the existing literature on morphological changes observed in myopic eyes.

Evaluation of Foveal Area and Vascular Density findings in our study, no statistically significant relationship was found between the FAZ area and AL. This finding is similar to previous studies by Min et al. (12) and Ucak et al. (13). Although FAZ measurement has been reported as a reliable follow-up tool in healthy eyes (14), the automatic calculation method of the OCT-A device used in our study, and the fact that the data were not separated into superficial and deep capillary plexuses, can be considered a limitation. While the literature discusses potential effects of age and sex on FAZ area (15, 16), the absence of significant demographic differences between our patient groups reduces the likelihood that our results were influenced by these factors.

However, a positive correlation was found between superficial foveal density (SFD) and deep foveal density (DFD) values and AL (SFD: p=0.005; DFD: p=0.016). This finding differs from other studies, such as Yang et al. (17), which reported a negative correlation between axial length and vascular density. We believe this difference may be related to optical magnification in eyes with high AL, which causes the imaging field to expand and thus results in higher-than-actual density values. As AL increases, magnification in the imaging system also increases. This can cause anatomical structures in OCT-A images to appear sparser than they actually are (18). However, since the device algorithms that calculate vascular density operate based on a fixed measurement area, ignoring this magnification effect may lead to the interpretation that vascular structures are closer together. Consequently, structures that are expected to be sparser may be erroneously reported as having higher density values. The default AL setting of 23.95 mm in the device used in our study may have made this artifact more pronounced in eyes with longer actual AL (19). The fact that most studies in the literature have examined only myopic groups and excluded eyes with short AL

may be another reason for the different results in our study. By including groups with a wide range of AL in these comparisons, our study makes an important contribution to the literature.

Relationship Between Neural Tissue Thickness and Axial Length in our results show that the thickness of the ganglion cell layer and inner plexiform layer (GCL+IPL) is negatively correlated with AL, and this relationship is statistically significant in all sectors ($p<0.05$). This finding is fully consistent with studies by Dhami et al. (21) and Tham et al. (20), which reported that mechanical stretching and retinal thinning due to axial elongation lead to a decrease in GCL+IPL thickness. Since GCL+IPL thinning may be an early indicator of glaucoma, our findings again emphasize the need for clinicians to consider axial length when interpreting these results in myopic patients.

Similarly, RNFL thickness also decreased with increasing AL. In particular, pRNFL thickness in the superior and inferior hemispheres, as well as in the nasal and inferior quadrants, showed a negative correlation with axial length ($p<0.05$). These results are similar to studies by Singh et al. (22) and Hashemi et al. (23), which suggested that the decrease in RNFL thickness is related to the spreading of nerve fibres over a larger area or mechanical damage due to stretching as a result of axial elongation. Some studies (24, 25) have found a positive correlation in the temporal quadrant within Asian populations; however, our study detected a different relationship in this quadrant. RNFL thickness was found to be significantly lower in the 23-23.99 mm AL group compared to both shorter and longer AL groups. This may indicate genetic or structural differences between populations.

Many studies in the literature have shown that as AL increases, the pRNFL and GCC become thinner. Our findings clearly demonstrate that in myopic eyes, RNFL and GCL+IPL thickness decrease with increasing axial length (22). This thinning is a physiological adaptation resulting from elongation of the eye. However, this presents an important challenge for clinicians: distinguishing the generalized thinning in a myopic eye from localized, pathological damage caused by glaucoma is crucial.

Limitations

The primary limitation of this study is the small number of patients with high AL (AL > 26 mm). This is due to factors such as the COVID-19 pandemic and a lower prevalence of high myopia in our population compared to Asian populations. This may have prevented us from fully determining the effect of axial elongation on vascular density. However, our study distinguishes itself from similar studies in the literature by including individuals with short AL, thereby comparing different AL groups. The OCTA device we used employs a default AL of 23.95 mm. If the actual AL differs from this, the device's image measurements will be inaccurate. This is the biggest limitation of our study.

Another limitation is that, although age is known to affect retinal parameters, we did not perform subgroup analyses based on narrower age ranges (e.g., 18-35, 36-49, 50-65 years). While we observed weak to moderate correlations ($r = -0.168$ to -0.409) between age and some parameters, no significant relationship was found between age and most parameters. Further grouping by age would increase the complexity of the results and reduce clarity. For this reason, detailed subgroup analyses based on age were not performed. Additionally, our study is cross-sectional and may not fully represent the general population.

Conclusion and Recommendations

This study has shown that evaluating the structural features of the retina and optic nerve head in different AL groups using OCT-A and other parameters is an important tool for understanding myopic changes. Our findings suggest that in highly myopic eyes, GCL+IPL and RNFL are significantly affected, and these changes may be related to mechanical factors caused by the elongation of the eye.

These results emphasize that axial length is a critical factor in the diagnosis and monitoring of diseases like glaucoma in myopic patients. Monitoring OCTA parameters is an effective tool to protect highly myopic eyes from myopic complications.

Future studies should validate these findings with larger patient groups and investigate the long-term effects of myopia progression on these parameters.

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